ORIGINAL ARTICLE

CLINICAL PROFILE AND RISK FACTORS LEADING TO RETINOPATHY OF PREMATURITY

Molugan M, Kumaravel KS

Abstract

Aim: To evaluate clinical profile and risk factors of retinopathy of prematurity (ROP) among infants admitted to a tertiary care hospital.

Materials & Methods: One year retrospective study of infants who met the criteria for ROP screening.

Results: Of 605 babies who underwent ROP screening, 200 (33%) babies were found to have ROP in various stages. There was a male preponderance (1.3:1). All infants with ROP weighed <2000 gm at birth, with 50.5%, 31% and 14.5% weighing between 1000 and 1500 gm, 1500 and 2000 gm, and less than 1000gms respectively. ROP was most commonly seen in Zone II (74%) and Zone I was the second most common (23%). The most prevalent postnatal risk factors among patients with ROP were respiratory distress syndrome (RDS) (57%) ($p<0.001$) and use of oxygen therapy (81%) ($p<0.001$). Forty three percent of infants with ROP had anemia of prematurity ($p<0.001$), while 26% of these infants required transfusion of packed red blood cells ($p<0.001$). Other significant postnatal risk factors were presence of sepsis (45%) ($p<0.001$), patent ductus arteriosus (12%) ($p<0.001$), hypoglycemia (17%) ($p<0.001$) and neonatal seizures (12%) ($p<0.001$). Of the 200 infants who developed ROP, 23 infants warranted laser photocoagulation in both eyes and 21 infants had a birth weight of less than 1500 gm.

Conclusion: The study underscores the importance of ROP screening of at risk neonates. The screening of infants above birth weight of 1750gms and 34 of week's gestational age should not be missed if they possess any of the risk factors. Neonates <1500gms are to be screened more effectively as need for laser photocoagulation was more seen in this group.

Introduction

Retinopathy of prematurity (ROP) is a significant cause of preventable blindness in children across both the developed and developing countries. (1-4) Prematurity has been regarded to be the most important risk factor of ROP, however, other factors such as low birth weight (LBW), high oxygen supplementation and its duration, respiratory distress syndrome (RDS), anemia, sepsis and blood transfusion were also found to have significant association. (5) Recent advancements in neonatal care and a massive impetus to neonatal care under the auspices of National Rural Health Mission in India have led to an increase in the survival of low birth weight and premature infants. (6) The improved survival of preterm and low birth weight infants has led to a rise of ROP incidence. (7,8) Globally, ROP is estimated to affect more than 50,000 infants annually and in India, every year, 500 children are estimated to become blind from ROP. (9) While ROP may cause severe visual impairments, the condition fortunately carries a good prognosis, given early screening and management. Thus, an effective screening protocol is essential for timely detection and treatment of this avoidable disease. (10) Moreover, there is a disparity between the profiles of ROP infants in developing countries when compared to developed countries, and no unified screening guidelines exist for ROP in India. If current American and British screening guidelines for ROP infants were applied in India, a large proportion of Indian infants would be missed because heavier infants (>1500 g) are also at a risk for developing ROP. (11)

The aim of the study is to evaluate the clinical profile and risk factors of ROP in the setting of a Neonatal Intensive Care Unit (NICU) at a tertiary care facility located in Tamil Nadu, India.

Methods & Materials

This is a retrospective study done in NICU of a tertiary care hospital between September 2016 and August 2017. All infants admitted to the NICU were screened for ROP after getting consent from the parents if they met the following criteria: (a) Presented at ≤34 weeks of gestation, (b) weighed ≤1750 g at birth, or (c) irrespective of birth weight and gestational age if possessed other significant risk factors such as sepsis, respiratory distress syndrome (RDS), or long-term oxygen use. Screening was performed by a retina specialist in the NICU under aseptic conditions, using an indirect binocular ophthalmoscope with a + 20 dioptre lens after pupillary dilatation.

The findings of the ophthalmic examination were documented as per the International Classification for Retinopathy of Prematurity (ICROP) recommendations specifying the location (Zone I–III) and severity of the disease (Stage I-V) with or without plus component and the extent of clock hours. (12)

Our treatment threshold was Stage III ROP disease or Stage II in Zone II with plus disease. All infants who qualified were treated with laser photocoagulation within 48 hours of diagnosis. Infants diagnosed with ROP were identified and any conditions that increased their risk of ROP development was recorded including mode of delivery, low birth weight, gestational age, history of sepsis, history of blood transfusion, history of transient tachypnea of the newborn (TTN), apnea of prematurity, oxygen therapy and respiratory support. Prenatal risk factors measured include multiple gestations and antenatal steroid use. The stage of ROP at the time of diagnosis, treatment intervention, was documented. Babies with congenital ocular anomalies, chorioretinitis and babies born after 36 weeks and whose birth weight was more than 2000gms were excluded from our study. Standard case definitions were used for all neonatal conditions. (13) The institutional ethical committee approval was obtained. Data was analyzed using R software version 3.4.2. All variables were summarized using frequency and percentages. To assess the strength of association between co-morbidities and presence of ROP in infants, Chi-square test was applied and Odds ratio was calculated as a measure of association. P-value was considered significant at 5% level of significance for all comparisons.

Results

A total of 5036 infants were admitted to the NICU between September 2016 and August 2017. Of 5036 infants, 605 babies underwent ROP screening. Two hundred (33%) out of 605 babies were found to have ROP in various stages. Patients with ROP showed a male predominance (1.3:1). The clinical parameters of gestational age, birth weight, stages of ROP and need for laser treatment is depicted in Table 1. Mean gestational age was 31+2.8 weeks and ranging from 26 to 36 weeks. The average gestational age among infants with severe ROP requiring laser treatment was 30+2.9 weeks ranging from 26 to 32 weeks gestational age. In the ROP group, 17 infants had a birth weight of more than 1750 gm and 21 infants were more than 34 weeks of gestational age. They were included in the study group as they had other significant risk factors. The most prevalent postnatal risk factors among patients with ROP were RDS and use of oxygen therapy. Fifty-seven percent of patients with ROP experienced RDS and 81% needed oxygen

Table 1: Clinical profile of infants with ROP

Variables	ROP (n=200)	ROP %	Required laser therapy (n=23)
Birth Weight (grams)			
<1000	29	14.5	3
1001-1500	101	50.5	18
1501-2000	62	31	2
2001-2500	8	4	0
>2500	0	0	0
Gestational Age (weeks)			
<28	14	7	8
28-32	109	54.5	11
32-36	72	36	4
>36	5	2.5	0
Stage of ROP			
Zone I	46	23	5
Zone II	148	74	18
Zone III	6	3	0

Table 2: Risk Factors associated with ROP

Comorbidities	Non ROP (n=405)	ROP (n=200)	P-value	Odd's Ratio	95% Confidence Interval
Sepsis	37 (9.1%)	91 (45%)	<0.001		
Transient tachypnea of newborn	62 (15.3%)	28 (14%)	0.670	0.90	0.56-1.46
Patent ductus arteriosus	11 (2.7%)	24 (12%)	<0.001	4.88	2.34-10.19
Anemia of prematurity	48 (11.9%)	86 (43%)	<0.001	5.61	3.72-8.47
History of blood transfusion	29 (7.2%)	52 (26%)	<0.001	4.56	2.78-7.45
Apnea of prematurity	53 (3.1%)	34 (17%)	0.197	1.36	0.85-2.17
Respiratory distress syndrome	61 (15.1%)	114 (57%)	<0.001	7.47	5.06-11.05
Oxygen therapy	61 (15.1%)	162 (81%)	<0.001	24.04	15.39-37.56
Respiratory support	37 (9.1%)	52 (26%)	<0.001	3.49	2.20-5.55
Neonatal seizures	18 (4.4%)	24 (12%)	0.001	2.93	1.55-5.54
Hypoglycemia	19 (4.7%)	34 (17%)	<0.001	4.16	2.31-7.51
Antenatal steroids	16 (4%)	18 (9%)	0.011	2.40	1.20-4.82
Multiple gestation	14 (3.5%)	28 (14%)	<0.001	4.55	2.34-8.85
Intraventricular hemorrhage	15(3.7%)	11 (5.5%)	0.30	1.51	0.68-3.36

therapy. Median duration of oxygen therapy required was 5 days (range: 1–42 days). Twenty six percent of patients required respiratory support via mechanical ventilation for an average of 3.5 days (range: 1 h–7 days). Forty three percent of infants with ROP were diagnosed with anemia of prematurity, while 26% of these infants required transfusion of packed red blood cells. Other significant postnatal risk factors noted were presence of sepsis (45%), transient tachypnea of the newborn (14%), apnea of prematurity (17%), patent ductus arteriosus (12%), hypoglycemia (17%) and neonatal seizures (12%). Multiple gestations were the most common prenatal risk factor with a prevalence of 14% among infants with ROP. Antenatal steroids were used in 9% of infants who developed ROP.

Of the 200 infants who developed ROP, 23 presented with severe enough disease warranting laser photocoagulation in both eyes. Twenty one out of these 23 infants weighed less than 1500gms. The average gestation age of these patients was 30 weeks (range: 26–32 weeks). All the 23 infants required oxygen therapy for an average of 10 days (range: 4–28 days). One half required respiratory support with an average length of 6 days on ventilation therapy (range: 4–8 days).

On comparison of co-morbidities (Table 2) between ROP and Non-ROP groups, the risk of development of ROP is significantly higher in infants with sepsis, patent ductus arteriosus (PDA), anemia of prematurity, oxygen therapy, respiratory support, multiple gestation, hypoglycemia and neonatal seizures ($p < 0.05$). On applying the odds ratio with 95% confidence interval, all the co-morbidities except TTN were significantly associated with development ROP with RDS and oxygen therapy having the highest odds ratio (Table 2).

Discussion

Severe ROP is a debilitating disease, which left untreated, may lead to permanent visual loss, resulting in decreased quality of life for the individual as well as a significant financial burden on the individual and the community. (14) In India, approximately, 1 in 1000 children is blind, and the incidence of ROP is reported between 24% and 47%. (15) Our study revealed a prevalence of ROP among preterm infants admitted to the NICU of a tertiary care hospital to be 33.06%.

The American and British guidelines recommend screening for ROP for all infants born ≤30 weeks gestational age or weighing ≤1500gms at birth. The guidelines further recommend that infants with birth weight of 1500–2000gms who experience an unstable course requiring cardiorespiratory support should also be screened. (16) All infants who developed ROP in our study weighed <2000gms at birth. In our study, 31% of infants with ROP were between 1500-2000gm and the overall average gestational age was 31 weeks.

Previous studies suggest that the use of antenatal steroids decrease the severity of ROP. (5) Our study found only eighteen cases of ROP among infants subjected to antenatal steroids (Table 2). In addition, studies have identified intraventricular haemorrhage (IVH) as an independent risk factor for the development of severe ROP. (17) In contrast, our study found only eleven cases of IVH among the infants who developed ROP, all of whom developed only Stage I disease and did not warrant intervention (Table 2). The small sample size of this study limits us to comment further on this potential phenomenon. More studies are needed to further evaluate the relationship between antenatal steroids and history of IVH with the development of ROP.

We found the incidence of ROP among multiple gestations to be 14%. The CRYO-ROP study showed the likelihood of developing threshold ROP disease to be 36% in multiple gestation birth. (18) Another Indian study from Telegana reported an incidence of 17%. (17)

The most prevalent postnatal risk factors among patients with ROP were RDS and use of oxygen therapy, followed by anemia of prematurity and sepsis. Sepsis can act by the release of cytokines and endotoxins secondary to infection. Its prevention and early treatment may reduce the incidence of ROP. The prevalence of these postnatal risk factors has not been clearly outlined in other studies. (17)

All the 23 infants who presented with severe ROP necessitating laser photocoagulation intervention required oxygen therapy and half required respiratory support. These results underscore the importance of screening in infants with these specific risk factors since they were highly associated with severe disease.

Conclusion

The study underscores the importance of ROP screening of at risk neonates. The screening of infants above birth weight of 1750gms and 34 weeks' gestational age should not be missed if they possess any of the risk factors. Neonates <1500gms are to be screened more effectively as need for laser photocoagulation was more seen in this group.

Funding : None

Conflict of Interest: None

References :

1. Tasman W. Retinopathy of Prematurity. Do we still have a problem? Arch Ophthalmol. 2011; 129:1083-6.
2. Azad R, Chandra P. Retinopathy of Prematurity. J Indian Med Assoc. 2005; 103: 370-2.
3. Coats DK, Miller AM, Hussein MA, McCreery KMB, Holz E, Paysee EA. Involution of Retinopathy of Prematurity after Laser treatment: Factors associated with developed of Retinal Detachment. Am J Ophthalmol. 2005; 140: 214-22.
4. Munoz B. Blindness and visual impairment in the Americans and the Caribbean. Br J Ophthalmol. 2002; 86:498-504.
5. Alajbegovic J, Zvizdic D, Alimanovichalilovic E, Dodik I, Duvnjak S. Risk Factors for Retinopathy of Prematurity in Premature Born Children. Med Arch Sarajevo Bosnia Herzeg. 2015; 69: 409-13.
6. Kumaravel KS, Ganesh J, Balaji J, Pugalendhiraja KV, Ramesh Babu B. A Study on Impact of NRHM on Neonatal

Care and Clinical Profile of Neonates Admitted in a SNCU of a Rural Medical College. Journal of Evolution of Medical and Dental Sciences 2015; 82(13):14335.
7. Miada JM, Mathers K, Alley CL. Pediatric ophthalmology in the developing world. Curr Opin Ophthalmol. 2008; 19: 403-8
8. Gilbert C, Fielder A, Gordillo L, Quinn G, Semiglia R, Visintin P. Characteristics of infants with severe retinopathy of prematurity in countries with low, moderate, and high levels of development: implications for screening programs. Pediatrics. 2005; 115: e518-25.
9. Gilbert C. Retinopathy of prematurity: A global perspective of the epidemics, population of babies at risk and implications for control. Early Hum Dev. 2008;84:77-82.
10. Gogia V, Gupta S, Patwardhan S, Azad R, Chandra P. Prevailing clinical practices regarding screening for retinopathy of prematurity among pediatricians in India: A pilot survey. Indian J Ophthalmol. 2011;59: 427-30.
11. 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; 55:331-336.
12. The International Classification of Retinopathy of Prematurity revisited. Arch Ophthalmol. 2005; 123:991-9.
13. National Neonatology Forum. Evidence based clinical practice guidelines, India, October 2010. Available on URL: www.nnfpublication.org. Accessed on 03.11.2017.
14. Mets MB. Childhood blindness and visual loss: An assessment at two institutions including a "new" cause. Trans Am Ophthalmol Soc. 1999; 97: 653-96.
15. 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: 687-9.
16. 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(6):189-95
17. 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 :119-122.
18. Mills MD. Evaluating the Cryotherapy for Retinopathy of Prematurity Study (CRYO-ROP). Arch Ophthalmol. 2007; 125: 1276-81.

From: Department of Pediatrics, Government Dharmapuri Medical College, Dharmapuri, Tamilnadu, India.

Address for Correspondence:
Dr. Kumaravel KS, Prof and Head, Department of Pediatrics, Government Dharmapuri Medical College, Dharmapuri, Tamilnadu 636007, India.

Email : kumaravelks@rediffmail.com
DOI : 10.7199/ped.oncall.2018.11