Original Article

Retinopathy of prematurity in babies weighing <1800 g; with special reference to babies weighing between 1501 and 1800 g: An experience from a tertiary care hospital in Delhi

Rohit Kapoor, Richa Talwar[1], Soumya Sachdeva[2], Premila Paul[3], Rakesh Yadav[2], Sarthak Sachdeva[4]

GDMO I, CGHS Dispensary D56, Government of India, Krishna Nagar, [1]Department of Community Medicine, Vardhman Mahavir Medical College and Safdarjung Hospital, [2]Intern, Vardhman Mahavir Medical College and Safdarjung Hospital, [3]Department of Pediatrics, Vardhman Mahavir Medical College and Safdarjung Hospital, Now In saket City Hospital, [4]VMMC and SJH, GDMO II, [5]Student, Maulana Azad Medical College, Bahadur shah zafar Marg, New Delhi, India

Address for the Correspondence:
Dr. Rohit Kapoor,
86-A Pocket F GTB
Enclave Opp. GTB Hospital,
New Delhi - 110 093, India.
E-mail: rohitvmmc@gmail.com

Access this article online

Website: www.ijmedph.org

DOI: 10.4103/2230-8598.144066

Quick response code:

Abstract

Background: Retinopathy of prematurity (ROP) is a disease related to low birth weight, prematurity, oxygen administration, and various other factors, which are yet to be identified. **Aims:** The aim was to find incidence of ROP and risk factors for causation in babies weighing <1800 g; and in the babies weighing between 1501 and 1800 g. **Design:** Prospective study. **Materials and Methods:** Neonates weighing ≤1800 g taking birth in our institution from January 2011 to January 2012 for a span of 1 year; were included in the study. The data were analyzed to determine risk factors for ROP causation. Information was collected using the standardized performa which included the maternal risk factors as well. Infants were classified by ophthalmologic examination findings using ICROP revisited. Statistics: Qualitative data were analyzed using Pearson's Chi-square test with Yates correction or Fisher's exact test and possible risk factors were analyzed by univariate analysis and multivariate analysis. **Results:** A total of 278 subjects was included in the study. Incidence of ROP in babies ≤1800 g was found to be 13.67% (38/278). Incidence of ROP in babies weighing between 1501 and 1800 g was 11.64% (17/146). Twenty-one risk factors were significant on univariate analysis in babies weighing ≤1800 g and 18 risk factors in the babies weighing between 1501 and 1800 g. Multiple gestations ($P < 0.01$), blood transfusion ($P < 0.01$), antepartum hemorrhage ($P < 0.01$), pregnancy-induced hypertension ($P < 0.01$), mechanical ventilation (MV) ($P < 0.01$), and APGAR at 1 min ($P < 0.01$) were found to be independently significant for ROP causation on logistic regression analysis in babies weighing ≤1800 g and MV ($P < 0.01$) and resuscitation ($P < 0.01$) were significant for babies weighing 1501-1800 g. **Conclusion:** It should be considered to incorporate screening of babies ≤1800 g uniformly in developing nations. It is recommended that further studies be done taking representative population of babies in different sites with adequate follow-up.

Key words: Birth weight, retinopathy of prematurity, risk factors

INTRODUCTION

Retinopathy of prematurity (ROP) is a disease related to low birth weight, prematurity, oxygen administration, and various other factors, which are yet to be identified.[1-4] It is a potentially blinding disorder in infants born prematurely. Incidence of ROP varies in different neonatal units.[5,7] It has been reported to vary from 21% to 65.8%[7-10] in western studies and 34.9-60.1%.[10,11] in Indian studies. The criteria laid by the AAP and AAPOS were based on CRYO-ROP Trial[12] and Light-ROP trial[13] which recommend screening infants with birth weight ≤1500 g or gestational age <28 weeks.[11] The scenario in the developed[4] and developing countries[5] however, differs. Low survival rate of very low birth weight and extremely low birth weight babies in rural and semi-urban areas, attribute to the said lower incidence of ROP in these babies; as seen in studies from Indian scenario. As a result; in the developing nations, infants with birth weight >1501 g are now more likely to develop ROP than their counterparts in western countries.[4,6] Although recent studies have reported increased incidence of ROP in babies >1501 g, most of the studies have not suggested their inclusion in the screening programs.

MATERIALS AND METHODS

This study was a prospective study conducted in a Medical College of Delhi in the Department of Pediatrics in collaboration with the Department of Ophthalmology for duration of 1 year from January 2011 to January 2012. A total of 278 neonates was included in the study. However, 203 neonates could complete the follow-up till the stipulated time period after being discharged from the nursery. The inclusion criteria included all the surviving neonates born at a tertiary care hospital in North Delhi weighing ≤1800 g. Babies who did not complete the follow up for any reason and with other ocular disorders, which interfere with fundus examination and those with other congenital retinal abnormalities were excluded. Prenatal, perinatal, and neonatal data were collected from each patient's medical record using a standardized data collection sheet for the study. The risk factors studied in this manner were birth weight, gestational age, respiratory distress syndrome (RDS), duration of oxygen exposure, acidosis, mechanical ventilation (MV), blood transfusion (BT), exchange transfusion (ET), anemia, sex, patent ductus arteriosus (PDA), resuscitation, APGAR score, intraventricular hemorrhage, antepartum haemorrhage (APH), premature rupture of membranes, maternal pre-eclampsia (PIH), neonatal hyperbilirubinemia, pneumothorax, intrauterine growth retardation (IUGR), multiple gestations, sepsis, vasopressor use. Information about risk factors for ROP and the maternal risk factors was obtained using a performa. The infants were classified by ophthalmologic examination findings using the Modified International Classification of ROP.[14] This location in this classification refers to how far the developing retinal vessels have progressed based upon three concentric zones, and severity of disease is predicted by five stages of the disease. The extent of disease is circumferential location of the disease, reported as clock hours in appropriate zones. Preplus, plus, aggressive posterior ROP are different spectrums of the disease.[14]

Prior approval was sought from the ethical review board of the institute and written consent was obtained from the parents, and they were explained the purpose of the study and were assured about the confidentiality and anonymity of the information so obtained. Screening was conducted in a temperature-controlled room in the presence of a pediatrician and ophthalmologist, and the cases of ROP were classified according to ICROP.[14] Qualitative data were analyzed using Pearson's Chi-square test with yates correction or fisher's exact test. At the completion of the study; the collected data were analyzed for postulated risk factors by univariate analysis. Multiple logistic regression analysis was performed to determine the independent effects of risk factors (which were found significant on univariate analysis) after controlling for confounding variables.

Table 1: Demographic profile of study population

Factors	*n* = 278	Percentage
Gestational age		
<32 weeks	58	20.86
32-36 weeks	160	57.55
>36 weeks	60	21.58
Sex		
<1800 g		
Male	144	51.799
Female	134	48.20
1501-1800 g		
Male	71	48.63
Female	75	51.37
<1500 g		
Male	63	47.73
Female	69	52.27

RESULTS

The demographic variables of the study population have been depicted in Table 1. The incidence was computed in babies weighing ≤1800 g and in 1501-1800 g. The incidence among the former was 13.67% (38/278) and in latter was found to be 11.46% (17/146). Distribution of ROP as per stage, gestation, and birth weight has been depicted in Table 2. It was found that maximum cases of ROP were reported among the babies <32 weeks of gestation; that is 32.76% (19/58) and further out of these; stage III ROP was reported in 1.72% (1/58), whereby in which active intervention in the form of laser therapy was done. The average gestational age of the babies weighing ≤1800 g and in 1501-1800 g was 33.13 ± 2.76 and 34.18 ± 2.09, respectively. The mean birth weight in babies weighing ≤1800 g and in 1501-1800 g was found to be 1510.072 ± 250.64 g and 1700.41 ± 88.96 g, respectively. The factors which were found to be significant on univariate and multivariate analysis in babies weighing ≤1800 g and 1501-1800 g have been depicted in Tables 3a and 3b, respectively. The ten most significant factors in babies weighing ≤1800 g include multiple gestations, anemia, MV, patent ductus arteriosus, and RDS on both univariate and multivariate analysis; and PDA, RDS, anemia,

Table 2: Incidence of ROP among the various subgroups. Gestation age and birth weight of the baby versus the stage of ROP

Incidence of ROP (any stage)	Weight			*n/N*	Percentage	
	<1800 g			38/278	13.67	
	1501-1800 g			17/146	11.64	
Stage of ROP	Gestation age			Birth weight		
	<32 weeks %	32-36 weeks %	>36 weeks %	≤1000 %	<1000-1500 g %	>1501-1800 g %
No ROP	67.24 (39/58)	89.95 (170/189)	100 (0/31)	72 (18/25)	86.92 (93/107)	88.36 (129/146)
Any stage of ROP	32.75 (19/58)	10.05 (19/189)	—	28 (7/25)	13.08 (14/107)	11.64 (17/146)

ROP: Retinopathy of prematurity

low APGAR at 5 min; on univariate analysis only. In the babies weighing between 1501 and 1800 g; the most important risk factors include anemia and BT; on multivariate analysis, and MV, acidosis, vasopressor use, intraventricular BT, sepsis, RDS, ET; on univariate analysis only. The odds of developing ROP due to above-mentioned risk factors have been depicted in the corresponding Table 3. The receiver operator response curve [Figures 1a and b] depicts that the risk factors among babies weighing <1800 g and 1501-1800 g could be depicted in 96% and 85.66% of the study population, respectively.

DISCUSSION

The present study was an attempt to find incidence and risk factors for ROP causation. It was found that the overall incidence of ROP

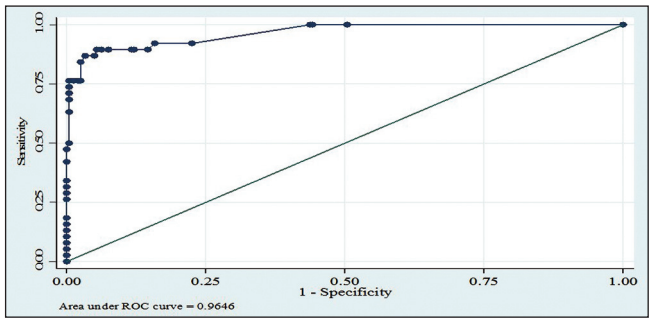

Figure 1a: The receiver operator curve depicts that the above model could discriminate the risk factors in 96% of the babies weighing <1800 g correctly

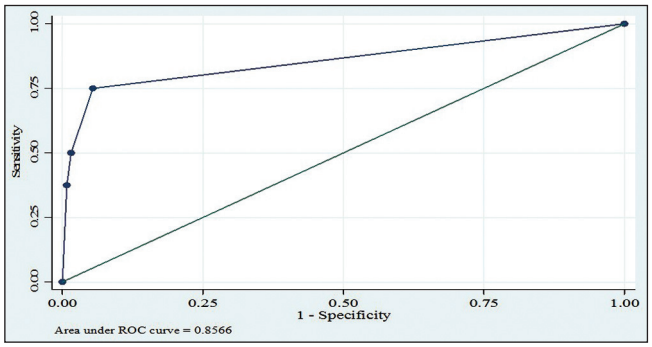

Figure 1b: The receiver operator response curve depicts that the model could discriminate the risk factors in 85.66% of the babies weighing between 1501 and 1800 g correctly

Table 3a: Univariate and multivariate analysis of risk factors in babies weighin ≤1800 g

Risk factor	ROP (absent = 240) (%)	ROP (present = 38) (%)	*P*	OR (95% CI)	Adjusted OR
Multiple gestation					
Singletons	230 (95.83)	14 (36.84)	0.001	39.4 (15.80-98.34)	52 (10.22-267.5)
Twins	10 (4.17)	24 (63.16)			
Blood transfusion					
Absent	227 (70.59)	20 (52.63)	0.0001	15 (6.73-36.66)	15 (3.8-66.2)
Present	13 (5.42)	18 (47.37)			
Ante-partum hemorrhage					
Absent	221 (92.08)	28 (73.68)	0.001	4 (1.75-9.82)	14 (1.66-120.7)
Present	19 (7.92)	10 (26.32)			
Maternal preeclampsia					
Absent	172 (71.67)	21 (55.26)	0.04	1.14 (0.68-1.90)	10.7 (2-53)
Present	68 (28.33)	17 (44.74)			
Mechanical ventilation					
Absent	231 (96.25)	18 (47.37)	0.0001	28 (11.1113-71.66)	10 (2.57-41.84)
Present	9 (3.75)	20 (52.63)			
Low Apgar score					
Absent	235 (97.92)	22 (57.89)	0.0001	6.4 (2.95-13.87)	5.9 (1.63-21.60)
Present	5 (2.08)	16 (42.11)			
Anemia					
Absent	172 (71.67)	21 (55.26)	0.04	34.18 (11.4-102.19)	
Present	68 (28.33)	17 (44.74)			
Patent ductus arteriosus					
Absent	239 (99.58)	35 (92.11)	0.001	20 (2.7-202.45)	
Present	1 (0.42)	3 (7.89)			
Respiratory distress syndrome					
Absent	197 (82.08)	8 (21.05)	0.0001	17 (7.36-40.06)	
Present	43 (17.92)	30 (78.95)			
Low Apgar score at 5 min					
<3	206 (85.83)	10 (26.32)	0.0001	17 (7.56-38.06)	
>3	34 (14.17)	28 (73.68)			

ROP = Retinopathy of prematurity, OR = Odds ratio, CI = Confidence interval

Table 3b: Univariate and multivariate analysis of risk factors in babies weighing 1501-1800 g

Risk factor	ROP (absent = 240) (%)	ROP (present = 38) (%)	*P*	OR (95% CI)	Adjusted OR
Anemia					
Absent	127 (94.1)	8 (5.9)	0.0001	71.43 (13.1-387.37)	24 (3.37-176.37)
Present	2 (18.2)	9 (81.8)			
Blood transfusion					
Absent	123 (95.3)	6 (4.7)	0.0001	37.58 (10.3-136.36)	16 (3.66-73.96)
Present	6 (35.3)	11 (64.7)			
Mechanical ventilation					
Absent	126 (93.3)	9 (6.7)	0.0001	37 (8.41-165.53)	10 (2.57-41.84)
Present	3 (27.3)	8 (72.7)			
Acidosis					
Absent	125 (93.3)	9 (6.7)	0.00001	27 (7.00-110.16)	
Present	4 (33.3)	8 (66.7)			
Vasopressor use					
Absent	128 (90.1)	14 (9.9)	0.0001	27.4 (2.67-281.75)	
Present	1 (25)	3 (75)			
Intraventricular hemorrhage					
Absent	128 (89.5)	15 (10.5)	0.003	17.06 (45-199.62)	
Present	1 (33.3)	2 (66.7)			
Blood transfusion					
Absent	128 (89.5)	15 (10.5)	0.0001	37.58 (10.3-136.36)	16 (3.66-73.96)
Present	1 (33.3)	2 (66.7)			
Sepsis					
Absent	105 (96.3)	4 (3.7)	0.0001	14.2 (4.2-47.45)	
Present	24 (64.9)	13 (35.1)			
Respiratory distress syndrome					
Absent	119 (93.7)	8 (6.3)	0.0001	13.3 (4.23-42.29)	
Present	10 (52.6)	9 (47.4)			
Exchange transfusion					
Absent	125 (91.2)	12 (8.8)	0.0001	13.02 (3.07-55.06)	
Present	4 (44.4)	5 (55.6)			

in babies weighing ≤1800 g was less as compared to various Western studies[7-10] and previous studies done in Indian scenario.[10,15] This study found low birth weight and low gestational age to be statistically significant for the causation of ROP; as also has been found by authors of previous studies.[5,8] The association of the prolonged oxygen exposure in babies weighing ≤1800 g on univariate analysis was detected; as also seen in previous studies.[17] RDS may result due to variations in oxygen fluctuation, alternating hypoxia, and hypercarbia; leading to ROP, which is in concordance with various studies done in Indian[19] and the western world.[20,21] The incidence of ROP was directly proportional to the length of time the tissue remains in acidotic state; these findings were concordant with data obtained in western[20,21] and Indian context.[16,18,23] MV due to variation in the oxygen tension was implicated as a risk factor; which is in accordance with various studies done by Yanovitch *et al.*[17] and Dogra *et al.*[16] MV was found to be independent risk factor in the causation of ROP [Table 3a] in infants weighing ≤1800 g. Similar finding was replicated by Yanovitch *et al.*,[17] Dogra *et al.*;[16] though on univariate analysis in babies weighing 1250-1800 g. Our present study of infants weighing ≤1800 g established a strong statistical association of BTs ($P < 0.0001$); similar to the studies done in the western context[17] and Indian context.[16,19] This study found anemia to be a significant risk factor, which is in concordance with the study done by Hammer *et al.*,[20] in which 37 out of 137 infants with anemia developed ROP. IUGR in the present study came out to be significant and had a protective influence on ROP However, study done by Prendville *et al.*[21] in 144 infants failed to find a significant co-relation between IUGR babies and ROP. Similarly, babies given extensive resuscitation with low APGAR scores <3 at 5 min had a significantly increased incidence of ROP due to virtue of tissue hypoxia and acidosis. Similar results were found in the studies done by Hammer *et al.*[20] The present study found PDA to be a significant risk factor in the causation of ROP in babies owing to increased delivery of oxygen to tissues; similar finding was endorsed by the studies done in Indian context[18] and western context.[20,21] Use of vasopressors was associated with increased risk of ROP due to vasoconstriction and tissue anoxia on the univariate analysis. Liu *et al.*[22] and Nair *et al.*[24] found use of dopamine to be significantly associated with ROP; both on univariate and logistic regression analysis. Our study concluded that the risk of ROP increases with multiple gestations on both univariate and multivariate analysis as it is known to increase the incidence of low gestational age, prematurity, and low birth weight. The maternal risk factors like APH had a significant association with ROP causation as seen in

studies of Indian context by Dogra *et al.*[16] and western context by Hammer *et al.*;[20] due to hypoxia and acidosis. Study done by Purohit *et al.*[23] found PIH to be significant risk factor; which was found to be significant in our study as well. Premature rupture of membrane had no effect on ROP causation; as was also seen by Higgins *et al.*[25]

CONCLUSION

Taking into consideration, the effects of various risk factors in ROP causation; we can conclude that ROP does occur in babies weighing between 1501 and 1800 g. Thus, the current policy of screening all babies below 1500 g and 32 weeks of gestation and those with birth weight between 1501 and 1800 g; only if risk factors are present must be continued. However, recommendations to extend the screening protocol in different hospitals and sites to examine different population strata should be put forth; given that there is the presence of a significant incidence of ROP in the birth weight range of 1501-1800 g; as has been found by our study.

ACKNOWLEDGMENT

The authors gratefully acknowledge the support of Dr. HarishChellani, Consultant and Professor and Dr. B. P. Gulliani Consultant and Professor Dr. K. C. Agarwal Head of Department Pediatrics and Dr. R. V. Azad, Professor and Head Dr. R. P. Centre of Ophthalmic sciences, AIIMS in the study.

REFERENCES

1. Azad RV, Chandra P. Retinopathy of prematurity-screening and management. Indian Med Assoc 2003;101:593-6.
2. Jalali S, Anand R, Kumar H, Dogra MR, Azad R, Gopal L. Programme planning and screening strategy in retinopathy of prematurity. Indian J Ophthalmol 2003;51:89-99.
3. Gilbert C, Rahi J, Eckstein M, O'Sullivan J, Foster A. Retinopathy of prematurity in middle-income countries. Lancet 1997;350:12-40.
4. Wagner RS. Increased incidence and severity of retinopathy of prematurity in developing nations. J Pediatr Ophthalmol Strabismus 2003;40:193.
5. Phan MH, Nguyen PN, Reynolds JD. Incidence and severity of retinopathy of prematurity in Vietnam, a developing middle-income country. J Pediatr Ophthalmol Strabismus 2003;40:208-12.
6. Charan R, Dogra MR, Gupta A, Narang A. The incidence of retinopathy of prematurity in a neonatal care unit. Indian J Ophthalmol 1995;43:123-6.
7. Fielder AR, Shaw DE, Robinson J, Ng YK. Natural history of retinopathy of prematurity: A prospective study. Eye (Lond) 1992;6:233-42.
8. Al-Essa M, Rashwan N, Al-Ajmi M. Retinopathy of prematurity in infants with birth weight above 1500 grams. East Afr Med J 2000;77:562-4.
9. Jandeck C, Kellner U, Kössel H, Bartsch M, Versmold HT, Foerster MH. Retinopathy of prematurity in infants of birth weight >2000 g after haemorrhagic shock at birth. Br J Ophthalmol 1996;80:728-31.
10. Deshpande DA, Chaturvedi M, Gopal L, Ramachandran S, Shanmugasundaram R. Treatment of threshold retinopathy of prematurity. Indian J Ophthalmol 1998;46:15-9.
11. Gopal L, Sharma T, Ramachandran S, Shanmugasundaram R, Asha V. Retinopathy of prematurity: A study. Indian J Ophthalmol 1995;43:59-61.
12. Cryotherapy for Retinopathy of Prematurity Cooperative Group. Multicenter trial of cryotherapy for retinopathy of prematurity. Snellen visual acuity and structural outcome at 5 1/2 years after randomization. Arch Ophthalmol 1996;114:417-24.
13. Reynolds JD, Hardy RJ, Kennedy KA, Spencer R, van Heuven WA, Fielder AR. Lack of efficacy of light reduction in preventing retinopathy of prematurity. Light Reduction in Retinopathy of Prematurity (LIGHT-ROP) Cooperative Group. N Engl J Med 1998;338:1572-6.
14. International committee for the classification of retinopathy of prematurity. The international classification of retinopathy of prematurity revisited. Arch Ophthalmol 2005;123:991-9.
15. Gopal L, Sharma T, Ramachandran S, Shanmugasundaram R, Asha V. Retinopathy of prematurity: A study. Indian J Ophthalmol 1995;43:59-61.
16. Dogra MR, Sanghi G, Zadeng Z, Vinekar A, Das P, Dutta S, *et al*. Maternal and neonatal risk factors for developing retinopathy of prematurity in preterm infants weighing greater that 1250 g at birth. AIOC Proceedings; 2009. p. 478-80.
17. Yanovitch TL, Siatkowski RM, McCaffree M, Corff KE. Retinopathy of prematurity in infants with birth weight ≥1250 grams-incidence, severity, and screening guideline cost-analysis. J AAPOS 2006;10:128-34.
18. Chellani H, Maini B,Guliani BP, Salhan S. Assessment of Risk Factors and Role of Antenatal Dexamethasone in Prevention of Retinopathy of Prematurity and its Severity. Thesis Submitted to University of Delhi, India;2002.
19. Dutta S, Narang S, Narang A, Dogra M, Gupta A. Risk factors of threshold retinopathy of prematurity. Indian Pediatr 2004;41:665-71.
20. Hammer ME, Mullen PW, Ferguson JG, Pai S, Cosby C, Jackson KL. Logistic analysis of risk factors in acute retinopathy of prematurity. Am J Ophthalmol 1986;102:1-6.
21. Prendiville A, Schulenburg WE. Clinical factors associated with retinopathy of prematurity. Arch Dis Child 1988;63:522-7.
22. Liu PM, Fang PC, Huang CB, Kou HK, Chung MY, Yang YH, *et al*. Risk factors of retinopathy of prematurity in premature infants weighing less than 1600 g. Am J Perinatol 2005;22:115-20.
23. Purohit DM, Ellison RC, Zierler S, Miettinen OS, Nadas AS. Risk factors for retrolental fibroplasia: Experience with 3,025 premature infants. National collaborative study on patent ductus arteriosus in premature infants. Pediatrics 1985;76:339-44.
24. Nair PM, Ganesh A, Mitra S, Ganguly SS. Retinopathy of prematurity in VLBW and extreme LBW babies. Indian J Pediatr 2003;70:303-6.
25. 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.

How to cite this article: Kapoor R, Talwar R, Sachdeva S, Paul P, Yadav R, Sachdeva S. Retinopathy of prematurity in babies weighing <1800 g; with special reference to babies weighing between 1501 and 1800 g: An experience from a tertiary care hospital in Delhi. Int J Med Public Health 2014;4:359-63.

Source of Support: Nil, **Conflict of Interest:** None declared.