International Journal of Current Research in Medical Sciences
ISSN: 2454-5716
P-ISJN: A4372-3064, E -ISJN: A4372-3061
www.ijcrims.com

Original Research Article

Volume 3, Issue 7 -2017

DOI: http://dx.doi.org/10.22192/ijcrms.2017.03.07.013

Incidence and Risk factors for Retinopathy of Prematurity in Neonates of weight ≤1.5 kg and/ or ≤32 weeks of Gestation in a tertiary care Hospital

Dr MS Pannu
Prof and Head, Department of Pediatrics, Govt. Medical College Amritsar
Dr Ashwani Kumar
Associate Professor, Department of Pediatrics, Govt. Medical College Amritsar
Dr Ravinder Singh
Junior Resident, Department of Pediatrics, Govt. Medical College Amritsar
Dr Karamjit Singh
Professor, Department of Ophthalmology, Govt. Medical College Amritsar
Dr. SPS Dhillon
Assistant Professor, Department of Pediatrics, Govt. Medical College Amritsar
Dr. Sehajpreet Singh
Medical Officer, Harvinder Hospital, Amritsar
Corresponding author: **Dr Ashwani Kumar**
Associate Professor, Department of Pediatrics, Govt. Medical College Amritsar, Punjab
Email : *sareen_ashwani@rediffmail.com*

Abstract

Introduction: Retinopathy of prematurity affects immature retinal vasculature of premature infants. India and other developing countries are facing the third epidemic of ROP. Various risk factors for development of ROP include low gestation, low birth weight, HMD, sepsis, shock, prolonged oxygen therapy, poor nutrition and weight gain, anemia, blood transfusion, IVH.

Objective: To determine incidence and risk factors of ROP in neonates of birth weight ≤ 1500 gm and/or gestation ≤32 weeks.

Methods: All the eligible neonates admitted in NICU at GMC, Amritsar from July 2014 to June 2015 were enrolled in this prospective observational study and all neonatal, antenatal and perinatal problems and treatments and interventions done in Neonates were recorded and screening for ROP was done by indirect opthalmoscopy at 4 weeks of postnatal age and followed up till retinal vascularization was complete. Data was analyzed statistically to find incidence and risk factors for ROP.

Results: Out of 77 babies screened, 31 babies were found to have ROP of which 9 babies required treatment. The incidence of ROP in this study was 40.3% .Risk Factors for ROP found significant on univariate analysis included birth weight, CPAP , mechanical ventilation, oxygen duration more than 10 days. blood transfusion, Hyaline

membrane disease , Apnea of prematurity, Anemia, BPD, duration of IV fluids for more than 10 days, attainment of full feed after 10 days. Apnea of prematurity was found to be independent risk factor for ROP in this study.
Conclusion : Of all the potential risk factors for ROP Apnea of prematurity was independent predictor of ROP.

Keywords: Retinopathy, ROP, ROP, univariate analysis .

Introduction

Retinopathy of Prematurity (ROP) is a vasoproliferative disorder affecting the retina of premature infants. The key pathological change in ROP is peripheral retinal neovascularisation[1]. It is one of the most common causes of visual loss in children and can lead to lifelong vision impairment and blindness.

ROP was first described by Terry in 1942, which was previously known as Retrolental Fibroplasia with implication of oxygen therapy as the causative agent[2]. ROP had been reported to have two epidemics in the past, in developed countries. The first epidemic occurred in 1940-1950s and unmonitored supplemental oxygen was the principal risk factor[3]. The second epidemic occurred during 1970-1980s, despite careful monitoring of oxygen delivery to neonates. It was concluded that this epidemic was due to increased survival of VLBW babies.

ROP is becoming a significant problem in developing countries and these countries are experiencing 3rd epidemic due to increased rate of preterm deliveries and NICU facility for these babies, but the lack of adequate resources and expertise to monitor blood gases and other variables is ultimately leading to increased ROP in these preterm babies[4]. Vision 2020 is a global initiative of the international agency for prevention of blindness where mission is the elimination of avoidable blindness by 2020[5]. Under this it was estimated that 60,000 children are blind due to ROP globally – Latin America being the region with the largest number. In addition, blindness due to ROP is likely to increase in India and China as their economies improve and NICU services expand[6,7]. The global initiative for the elimination of avoidable blindness targets ROP for prevention and treatment in an effort to decrease the prevalence of childhood blindness.

India shares 20% of the world's childhood blindness[8]. ROP affects over 3,00,000 infants worldwide[8]. In developing countries like India, the incidence of ROP has been reported at 24-47% among high risk preterm infants[9]. Incidence of treatable or threshold ROP reported in India vary from 10.2-11% as reported by Hungi et al and Jalali et al to 44.9% as reported by Vinekar et al[10,11,12]. Recent studies from good quality tertiary institutions have reported ROP incidence from 11.9% to 22%(Kumar P et al and Chaudhari S et al)[13,14].

Higher incidence of severe ROP in more mature and bigger babies (mean birth weight 1488 gm for threshold ROP) has been reported by Shah et al [15]. Sanghi et al reported aggressive posterior ROP (APROP) in infants more than 1500 gm in our country [16].

Although supplemental oxygen therapy has been considered the main risk factor in the past, several recent studies have suggested a multifactorial basis for ROP development. The risk factors reported in different studies [17,18,19] are very low birth weight, prolonged mechanical ventilation, repeated blood transfusion, septicemia, hyperoxia/hypoxaemia, hypotension, acidosis, apnea treated by bag and mask ventilation, oxygen duration for more than 7 days, respiratory distress syndrome, anemia, patent ductus arteriosus, phototherapy , type of feeding. Poor postnatal weight gain and intrauterine growth retardation has also been implicated as a risk factor for ROP as reported by Hellstrom A et al [20].

With neonatal units being equipped with the state of art technology and highly qualified personnel providing optimum care to extremely immature

newborns, ROP incidence is on the rise. By early detection and timely intervention, blindness due to ROP is preventable. The purpose of this study was to know the incidence and to find maternal and neonatal risk factors for ROP in VLBW infants.

Materials and Methods

This prospective study was conducted in NICU, Department of Pediatrics ,Govt. Medical College, Amritsar, in collaboration with Department of ophthalmology on infants with birth weight of less than or equal to 1500 gm and or gestation less than or equal to 32 weeks from July 2014 to June 2015. The study was conducted after taking permission from the ethics committee, Government Medical College Amritsar and informed consent was taken from parents/guardians. Total two hundred and twenty seven neonates were admitted. 150 babies could not be screened due to death, exclusion due to congenital malformations and loss to follow up. 77 infants were followed up as per protocol and included in the study. On admission, babies were examined and managed as per existing medical conditions and unit protocol. The babies were weighed, gestational age was assessed, other clinical information was recorded which included the gender, mode of delivery, neonatal risk factors i.e. birth asphyxia, sepsis, apnea, NEC, HIE, pneumonia, hyperbilirubinemia, seizures, meningitis, HMD and treatment modalities given to babies were recorded i.e. any use and duration of supplemental oxygen, phototherapy, surfactant, exchange transfusion, blood transfusion, IVF, type of feeding, CPAP, mechanical ventilation.

Detailed Eye examination of all the babies were conducted by a single ophthalmologist at 4 weeks postnatally or 32 weeks post-conceptional age whichever was earlier. Pupilary dilatation was achieved with a mixture of 2.5% phenylephrine and 0.5% tropicamide instilled 3 times before the scheduled examination. Topical anaesthetic 2% proparacaine was used. The examination was done using an indirect ophthalmoscope with 20 D lens or 28 D lens. The retinal findings were recorded as per guidelines of ICROP. Follow up examinations were conducted until full vascularization of retina reached zone 3 or until full remission of ROP after Laser treatment.

Data was analyzed using SPSS statistical package. The incidence of ROP was calculated in simple proportion. By using the chi-squared test, Univariate analysis of risk factors for ROP was done. A logistic regression model was performed to find independent risk factors for ROP which were shown to be significant on univariate analysis. A probability (p) of less than 0.05 was considered significant.

Results

This study was conducted in the Department of Pediatrics in collaboration with Department of ophthalmology, Government Medical College Amritsar. Out of 77 babies screened , 31 babies were found to have ROP of which 9 babies required treatment. The incidence of ROP in this study was 40.3% (Table 1) .Out of 31 babies with ROP, 23 babies (74.19%) had stage 1 ROP, 5 babies (16.13%) had stage 2 ROP and 3 (9.68%) babies had stage 2 or 3 with plus disease (Table 2).

Table 1: Incidence of ROP

ROP	No.	%
PRESENT	31	40.3%
ABSENT	46	59.7%
TOTAL	77	100

Table 2: Stages of ROP

	RETINOPATHY OF PREMATURITY			
	STAGES			
	1	2	2 or 3 with	TOTAL
ROP PRESENT	23	05	03	31
%	74.19%	16.13%	9.68%	100%

43 babies were male and 34 were females out of total 77 babies. Out of 31 babies with ROP 18 were males and 13 were females. Total 18 babies had weight less than 1 kg out of which 16(89%) had ROP. Out of 24 babies with weight between 1 kg to 1.25 kg 11(45.8%) had ROP. In weight category between 1251 gm to 1500 gm 3 babies out of 32 had ROP. Out of 3 babies which were more than 1500 gm only 1(33.3%) had ROP. Mean birth weight of babies with ROP was 1069 gm while mean birth weight of babies without ROP was 1328 gm. Low birth weight was significantly associated with ROP (p=0.000).

Risk Factors for ROP found significant on univariate analysis included birth weight (mean birth weight 1069 and 1328 in ROP and no ROP group respectively) (P=0.000), CPAP (p=0.000), mechanical ventilation (p=0.044), oxygen duration more than 10 days (p=0.005). blood transfusion (p=0.004),OR 4.086, Hyaline membrane disease (p=0.004) OR 5.775, Apnea of prematurity (p=0.000) with OR 13.263, Anemia (p=0.002) OR 5.223, BPD (p=0.012), duration of IV fluids for more than 10 days (p=0.036) OR 3.00,attainment of full feed after 10 days(p=0.005) OR 3.92 (table 3 and 4).

Table 3: Neonatal morbidities as Risk Factors for ROP

Neonatal complications	ROP				p value
	Absent(n=46)		Present(n=31)		
	No.	%	No.	%	
1.PDA	2	4.3	2	6.5	0.683
2.NEC	8	17.4	6	19.4	0.827
3.Pneumonia	1	2.2	2	6.5	0.341
4. Meningitis	6	13.0	3	9.7	0.652
5.Intracranial Hemorrhage	1	2.2	0	0	0.409
6. Apnea of prematurity	19	41.3	28	90.3	0.000
7. Sepsis	37	80	28	90	0.241
8. Shock	8	17.4	5	16.1	0.885
9. Hypothermia	1	2.2	3	9.7	0.146
10. BPD	0	0	4	12.9	0.012*
11. Asphyxia	11	23.9	6	19.4	0.636
12. Hypoglycemia	13	28.3	3	9.7	0.111
13 .Resuscitation required	7	15.2	4	12.9	0.776
14.Anemia	7	15.2	15	48.4	0.002
15. Surfactant	5	10.9	2	6.5	0.508
16.HMD	4	8.7	11	35.5	0.004

Table 4 : Neonatal Interventions as Risk Factors for ROP

Neonatal complications	ROP				P value
	Absent (n=46)		Present (n=31)		
	No.	%	No.	%	
1. O2 duration >10 days	10	22.7	17	54.8	0.005
2.CPAP	20	45.5	27	87.1	0.000
3.Ventilation	9	19.6	13	41.9	0.044
4.Blood Transfusion	19	41.3	23	74.2	0.004
5. Umbilical Catheter	7	15.2	7	22.6	0.414
6. IV fluid > 10 days	8	17.4	12	38.7	0.036
7.Full feed >10 days	12	26	18	58ss	0.005
8..Exchange Transfusion	1	2.2	0	0	0.409

Maternal risk factors like pregnancy induced hypertension, gestational diabetes, placenta previa, antepartum hemorrhage, antenatal steroids, anemia in mother were studied but none of the factors was found to be statistically significant.

PDA, NEC, pneumonia, meningitis, Intracranial hemorrhage, HIE, hyperbilirubinemia, seizures, hypothermia, asphyxia, hypoglycemia, resuscitation at birth, umbilical catheterization, surfactant, phototherapy and exchange transfusion were not significantly associated with incidence of ROP.

On Multivariate logistic analysis of various risk factors which were significant on univariate analysis apnea of prematurity was found to be independent risk factor for ROP in this study (table 5).

Table 5 : Multivariate analysis of risk factors for ROP

Risk factors	Adjusted Odds ratio	*P* value	95% CI
APNEA	8.130	0.004	1.975 – 33.464
ANEMIA	2.219	0.268	0.542 – 9.086
IV FLUIDS DURATION	0.812	0.800	0.162 – 4.068
ATTAINMENT OF FULL FEED	1.551	0.588	0.317 – 7.577
TRANSFUSION	1.406	0.635	0.344 – 5.746
HMD	1.520	0.585	0.338 – 6.830

Discussion

Retinopathy of prematurity (ROP) is a vasoproliferative disorder and among the preventable causes of blindness in children, ROP figures very high in the agenda.

We screened 77 babies admitted to our NICU with birth weight ≤ 1500g and/or gestation ≤ 32 weeks. Out of these 31 babies were found to have ROP, 9 of whom required treatment and rest underwent spontaneous regression. Out of 31 babies with ROP, 23 babies (74.19%) were in stage 1, 5 babies (16.13%) were in stage 2 and 3 (9.68%) babies developed stage 2 or 3 with plus disease. The overall incidence of ROP in the present study was 40.3%.

Various Indian studies had reported overall incidence ranging from 17.5% to 46% and International studies ranging from 10.0% to 45.4%. Maheshwari et al in 1996 reported overall incidence as 20% and severe ROP as 7% in 66 babies with gestation <35wk or < 1500g [21]. Patil et al in 1997 reported overall incidence as 17.5% and no severe ROP in 40 babies with gestation <32wk or < 1250g [22]. Gupta et al in 2003 reported overall incidence as 21.7% and severe ROP as 5% in 60 babies with gestation ≤ 35wk or ≤1500g[23]. Dutta et al in 2004 screened 108 babies of ≤32 week or ≤1700g and reported overall incidence as 21%[24]. Chaudhari et al in 2009 reported overall incidence of 22.3% in 552 babies with ≤32 weeks and birth weight <1500 g [14].

However, in recent years due to improved awareness about ROP, saturation targets, focus on prevention and routine screening as well as advanced treatment options, the morbidity associated with ROP has been found to be decreasing. Aggarwal et al found a drop from 46 to 21% in their study over a period of 7 years[25]. In 2000 a Danish study found a statistically significant decrease in incidence of ROP in infants weighing more than 1250g[26]. Similar observations were also made in a multicentre study in UK[27]. However, in most instances, it was not possible to compare studies, as the inclusion criteria , unit protocol and quality of care was different in different units.

Risk Factors for ROP found significant on univariate analysis included birth weight (mean birth weight 1069 and 1328 in ROP and no ROP group respectively), CPAP, mechanical ventilation, oxygen duration more than 10 days. blood transfusion, Hyaline membrane disease, Apnea of prematurity , Anemia, duration of IV fluids for more than 10 days, attainment of full feed after 10 days.

In our study, AOP was found to be an independent risk factor for ROP on multivariate analysis (p=0.001). Similar results were shown by Agarwal et al and Gupta et.al [25,23]. In the present study, oxygen duration >10 days, C-PAP and ventilation were found to be significant risk factor on univariate analysis similar to results shown by shah et al in their study on ROP in 2005 [28] . A study by Seiberth V et al showed that artificial ventilation for more than 7 days was a risk factor associated with higher rates of ROP [29].

Lower birth weight and gestation is a known risk factor for ROP. Multicenter Trial of Cryotherapy showed that lower the birth weight, the greater the risk of developing ROP especially at birth weights less than 750 g [30]. In another study, in 2001 Dogra et al reported that 30.7% of babies with threshold ROP treated with cryotherapy were more than 1250 g and 15.3% were more than 1500 g at birth [31].

In our study, HMD was found to be a significant risk factor for the development of ROP. Vinekar et al also showed HMD to be a significant risk factor for the development of ROP [12]. Kumar P et al also found HMD, PDA and meningitis as independent risk factor for ROP [13]. Sepsis was not significantly associated with the development of ROP in this study which is in contrast to study conducted by Vinekar et al[12].Blood transfusion was found to be a significant risk factor for the development of ROP in our study. In 2004 Dutta et al also reported that packed cell transfusion and double volume exchange transfusion as a major risk factor for ROP [24]. In our study, we found that BPD was significantly associated with the development of ROP. Similar studies by Sabzehei et al in 2013 and Gonçalves et al in 2014 also showed BPD to be a significant risk factor for the development of ROP [32,33].

IV fluid for more than 10 days and not attaining full feed by day 10 of life was also significant risk factor on univariate analysis though not a independent risk factor. Impact of nutrition and postnatal weight gain on ROP has also been emphasized by Hellstorm A et al [20].

Different units have reported varying risk factors but low gestation, lower weight and associated morbidities of prematurity are usual denominators. As of now In India we are facing third epidemic due to more preterm births, increased survival of preterms, unregulated and unblended oxygen, less awareness in pediatricians about saturation targets, ROP screening and lack of trained ophthalmologists. There should be focus on prevention with target saturation in babies <28 weeks as 90-95% and in more mature babies in range of 88-93%. Pediatricians and Neonatal nurses should focus on prevention of ROP by asepsis, breast milk, target saturations, optimum nutrition, timely screening and diagnosis and laser therapy if required.

Conclusion

Incidence of ROP was 40.3% with 8.5% neonates requiring Laser treatment. Apnea of prematurity was an independent risk factor for ROP. Timely screening and Laser treatment is recommended. Role of Pediatricians and Neonatal Nurses in prevention and screening for ROP is critical.

References

1. Charan R, Dogra MR, Gupta A, Narang A. The incidence of retinopathy of prematurity in a neonatal care unit. Indian J Opthalmol 1995; 43: 123-6.
2. Terry TL. Extreme prematurity and fibroblastic overgrowth of persistent vascular sheath behind each crystalline lens. I. Preliminary report, Am J Ophthalmol 1942; 25 : 203-04.
3. Clare Gilbert. Retinopathy of Prematurity: A global perspective of the epidemics, population of babies at risk and implications for control. Early Human Development 2008; 84: 77-82.
4. Gilbert C, Rahi J, Eckstein M, O'Sullivan J, Foster A. Retinopathy of prematurity in middle-income countries. Lancet 1997; 350: 12-4.
5. Gilbert C, Foster A. Childhood blindness in the context of vision 2020 – the right to sight. WHO Bulletin 2001; 79: 227-32.
6. Guidelines for retinopathy of prematurity screening and treatment in latin. American countries. Childhood Blindness Subcommittee, LA IAPB.
7. Tyetors B. A global initiative for elimination of avoidable blindness. American Journal of Ophthalmology 1998; 125: 90-3.
8. Global initiative for the elimination of Avoidable blindness Action Plan 2006-2007.
9. Reza S. Prevalence and Predisposing factors of Retinopathy of prematurity in very- birth-weight infants discharged from NICU. Iran J Pediatr 2009; 19(1): 59-63.
10. 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;79:911-15
11. Jalali S, Matalia J, Hussain A, Anand R. Modification of screening criteria for retinopathy of prematurity in India and other middle-income countries. Am J Opthalmol 2006;141:966-968.
12. 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 Opthalmol 2007;55:331-336
13. Kumar P, Sankar MJ, Deorari A, Azad R, Chandra P, Aggarwal R et al .Risk factors for severe ROP in preterm low birth weight neonates. Indian J Pediatr.2011 Jul;78(7):812-6
14. Chaudhari S, Patwardhan V, Vaidya U, Kadam S, Kamat A. Retinopathy of Prematurity in a Tertiary Care Center, Incidence, Risk Factors and Outcomes. Indian Pediatr 2009;46:219–24.
15. Shah PK, Narendran V, Kalpana N, Gilbert C. Severe retinopathy of prematurity in big babies in India: History repeating itself ? Indian J Pediatr 2009;76:801-804

16. Sanghi G, Dogra MR. Katoch D, Gupta A. Aggressive posterior retinopathy of prematurity in infants >1500 gm birth weight. Indian J Opthalmol 2014;62:254-7.
17. Keith CG, Doyle LW, Kitchen WH. Retinopathy of prematurity in infants of 24-30 weeks gestational age. Med J Aust 1989;150:213-6.
18. Valentine PH, Jackson JC, Kalina RE. Increased survival of low birth weight infants: Impact on the incidence of retinopathy of prematurity. Pediatrics 1989;84:442-5
19. Phelps, DL: Retinopathy of prematurity: an estimate of vision loss in the United States - 1979. Pediatrics 1981; 67: 924-6.
20. Hellstrom A, Engstrom E, Hard AL. Postnatal serum insulin-like growth factor-I deficiency is associated with retinopathy of prematurity and other complications of premature birth. Pediatrics.2003;112 : 1016-20.
21. Maheshwari R, Kumar H, Paul VK, Singh M, Deorari AK, Tiwari AK. Incidence and risk factors of Retinopathy of Prematurity in a tertiary care newborn unit in New Delhi. Natl Med J Ind 1996; 9(5): 211-4.
22. Patil J, Deodhar J, Wagh S, Pandit AN. High risk factors for development of retinopathy of prematurity. Indian Pediatrics 1997; 34: 1024-7.
23. Gupta VP, Dhaliwal U, Sharma R, Gupta P, Rohatgi J. Retinopathy of Prematurity - Risk factors. Indian J Pediatrics 2004; 71:887- 92.
24. Dutta S, Narang A, Dogra M, Gupta A. Risk factors of threshold retinopathy of prematurity. Indian Pediatrics 2004; 41: 665-71.
25. Agarwal R, Deorari AK, Azad RV, Kumar H, Talwar D. Changing Profile of Retinopathy of Prematurity. J Tropical Paediatrics 2002; 48:239 - 42.
26. Fledelius HC, Dahl H. Retinopathy of Prematurity, a decrease in frequency and severity. Trends over 16 years in a Danish county. Acta Ophthalmol Scand 2000; 78: 359-61.
27. Lee S, Charles BA, Millan, Ohlesson, Vincu M, Christopher. Evidence for changing guidelines for routine screening for retinopathy of prematurity.Archives Pediatrics and Adolescent Medicine 2001; 155(3): 387-95.
28. 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.
29. Seiberth V, Linderkamp O. Risk factors in retinopathy of prematurity. a multivariate statistical analysis. Ophthalmologica 2000; 214(2):131–5.
30. Palmer EA, Flynn JT, Hardy RJ. Incidence and early course of retinopathy of prematurity. Ophthalmology 1991;98:1628–40.
31. Dogra MR, Narang S, Biswas C, Gupta A, Narang A. Threshold retinopathy of prematurity: Ocular changes and sequelae following cryotherapy. Indian J Ophthalmol 2001; 49: 97-101.
32. Sabzehei MK, Afjeh SA, Dastjani Farahani A, Shamshiri AR, Esmaili F. Retinopathy of prematurity: Incidence, risk factors, and outcome. Arch Iran Med 2013; 16(9): 507-12.
33. Gonçalves E, Násser LS, Martelli DR, Alkmim IR, Mourão TV, Caldeira AP et al. Incidence and risk factors for retinopathy of prematurity in a Brazilian reference service. Sao Paulo Med J 2014; 132(2): 85-91.

How to cite this article:
MS Pannu, Ashwani Kumar, Ravinder Singh, Karamjit Singh, SPS Dhillon, Sehajpreet Singh. (2017). Incidence and Risk factors for Retinopathy of Prematurity in Neonates of weight ≤1.5 kg and/ or ≤32 weeks of Gestation in a tertiary care Hospital. Int. J. Curr. Res. Med. Sci. 3(7): 75-82.
DOI: http://dx.doi.org/10.22192/ijcrms.2017.03.07.013

Access this Article in Online
Website: www.ijcrims.com
Subject: Medical Sciences
Quick Response Code