Original Research Article

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A retrospective study on the risk factors for retinopathy of prematurity in NICU of tertiary care hospital

Sundar K. C.1, Devi Meenakshi K.1*, Aruna B. Patil²

¹Department of Paediatrics, Government Kilpauk Medical College, Chennai, Tamil Nadu, India ²Department of Community Medicine, ESIC Medical College, Chennai, Tamil Nadu, India

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*Correspondence: Dr. Devi Meenakshi K.,

E-mail: drdevi_1804@yahoo.in

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ABSTRACT

Background: Retinopathy of prematurity (ROP) affects developing retinal vasculature in premature infants. The risk factors for ROP are prematurity, low birth weight, oxygenation, respiratory distress, infection and frequent blood transfusion. Identification of risk factors leading to ROP may help in planning preventive strategies.

Methods: A retrospective analysis of records of preterm babies less than 34 weeks of gestation or birth weight less than 1750 grams and between 34 -36 weeks gestation or 1750-2000 grams birth weight associated with risk factors for ROP admitted to NICU of Kilpauk Medical college hospital from August 2015 to July 2016 were evaluated.

Results: Out of a total of 166 babies who were screened for ROP, 37 babies were detected to have ROP (22.3 %). Of these 20 (54%) were female and 17 (46%) were male. The mean birth weight of babies with ROP identified in our study was 1480 grams. The mean gestational age of babies with ROP was 32 weeks. By logistic regression analysis for mode of oxygen therapy as a risk factor for ROP it was found that prongs alone showed the strong risk factor towards ROP which was statistically significant. Sepsis, transfusion and shock requiring inotropes individually and statistical significantly contributed to the risk of ROP.

Conclusions: ROP was more common in babies <34 weeks. Sepsis, transfusion and shock requiring inotropes significantly contributed to the risk of ROP. Analysis of the mode of oxygen therapy showed that use of prongs significantly increased the risk of ROP.

Keywords: Risk factors, Retinopathy of prematurity, Sepsis, Transfusion

INTRODUCTION

Retinopathy of prematurity(ROP) is one of the chronic morbidities that occur in preterm neonates. As neonatal care services have improved over the years more and more of extreme preterm babies survive.

Our focus in neonatal care has been modified from one of measures to prevent death in neonates to providing quality survival in the babies who are discharged from the neonatal unit. This calls for a structured follow up programme that will screen these babies early in order to prevent visual handicap. Needless to say, that permanent visual loss from ROP is one of the most dreaded handicaps a neonate can have. More and more knowledge on the risk factors leading to ROP can help to prevent the occurrence of the problem.

Screening for ROP has now become a part of the neonatal care offered to the baby even before discharge. Several studies have shown that there is a wide variation in the timing of ROP and the risk stratification of babies who are vulnerable. This calls for studies to identify the high risk factors in our population to enable us to plan measures to limit the morbidity.

Retinopathy of prematurity is defined as a complex disease of the developing retinal vasculature in premature infants.¹ The clinical manifestations range from mild changes to severe disease with complications like retinal detachment.¹ There is an alarming increase in the incidence of retinopathy of prematurity in developing countries.² The improved survival of preterm and small-for-date neonates in developing countries has led to an increase in the incidence of retinopathy of prematurity in infants. Analysis of risk factor may help to predict the development of ROP.³

The principal risk factors for ROP are prematurity, oxygenation, respiratory distress, infection, hypercarbia, acidosis, anemia, and the need for transfusion. The risk of ROP increases with gestational age <28 weeks and birth weight <1000 gms.4 Importance of the screening should not be underestimated, as early detection and treatment reduces blindness and permanent disability. The most important determinant of any ROP management program is an effective screening strategy². 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 NNF 2010 Guidelines screening for ROP is recommended for babies born before 34 weeks of gestation or less than 1750 grams birth weight and babies born between 34-36 weeks of gestation or 1750-2000 grams birth weight if they have risk factors for ROP (mechanical ventilation, prolonged oxygen therapy and hemodynamic instability).⁶

METHODS

It was a retrospective analysis of medical records of preterm neonates treated in the NICU of Kilpauk Medical College hospital from August 2015 to July 2016. All the preterm infants less than 34 weeks of gestation or birth weight less than 1750 grams were included in the

analysis. Preterm infants between 34 -36 weeks gestation or 1750-2000 grams birth weight with any one of the known risk factors for ROP like mechanical ventilation, perinatal asphyxia, sepsis, prolonged oxygen therapy and hemodynamic instability, repeated blood transfusion were also evaluated. Babies who died before ROP screening, babies with congenital anomalies and babies with inborn errors of metabolism were excluded from the study. The following parameters were analysed and they include gestational age, birth weight, blood transfusion, duration of CPAP therapy, duration of mechanical ventilation, duration of oxygen therapy by nasal prongs or hood, co morbid conditions, sepsis and asphyxia. All preterm babies who satisfied the inclusion criteria were routinely screened by a single experienced ophthalmologist at 31 weeks of gestation or between 4-6 weeks of chronological age during the NICU stay and on high risk baby follow up clinic visit. After initial screening examination further follow up was done every week until ROP regressed or warranted laser therapy. Babies who had been detected with stage 3 ROP or with evidence of plus disease were managed with Laser therapy. Follow up was given in high risk baby follow up clinic.

The results of qualitative data were presented in frequency and percentage. The Chi square test was used to test the association between risk factors and ROP. The risk was measured by Odds ratio and estimated it with 95%CI for all risk factors. To predict the role of dependent variable ROP in respective with independent variables, the logistic regression has been used. The statistical significance was considered at p <0.05. The statistical analysis was done by using SPSS (version 21.0).

RESULTS

For this study, a total of 166 babies were screened in order to detect ROP positive cases during the period August 2015 to July 2016. The prevalence of ROP in this study was 22.3%.

Table 1: Demographic profile among bables screened for KOr.	

Danamatana		ROP				
Parameters	Category	Yes	No	Total (n=166)	P value	
Sex	Male	17 (46%)	72 (56%)	89 (54%)	0.200*	
	Female	20 (54%)	57 (44%)	77 (46%)	0.289*	
Costational	<34 weeks	26 (70%)	71 (55%)	97 (58%)	0.097*	
Gestational age	≥34 weeks	11 (30%)	58 (45%)	69 (42%)	0.097**	
Dinth waight	<1750 gms	23(62%)	71 (55%)	94 (57%)	0.441*	
Birth weight	≥1750 gms	14 (38%)	58 (45%)	72 (43%)	0.441	

^{*}not significant

Out of the 37 babies who were detected to have ROP, 20 (54%) were female and 17 (46%) were male. Analysis of the gestational age revealed that 26 (70 %) babies with ROP were less than 34 weeks of gestation and 11 (30%)

babies with ROP were more than 34 weeks gestation. When categorized by birth weight, it was observed that the 23 babies (62%) with ROP were less than 1.75 kg birth weight. Among babies with birth weight more than

1.75 kg, there were 14 babies (38%) with ROP. In present study though there were more babies with less than 34

weeks and <1750 grams birth weight this was not statistically significant (Table 1).

Table 2: Association of individual risk factors among babies screened for ROP.

Risk factors		ROP			
	Response	Yes (n=37)	No (n= 129)	Total (n=166)	P value
Dieth Amburia	Yes	8 (22%)	27 (21%)	35 (21%)	0.92
Birth Asphyxia	No	29 (78%)	102 (79%)	131 (79%)	
Sanaia	Yes	28 (76%)	41 (32%)	69 (42%)	<0.0001***
Sepsis	No	9 (24%)	88 (68%)	97 (58%)	
Transfusion	Yes	21 (57%)	25 (19%)	46 (28%)	<0.0001***
Transfusion	No	16 (43%)	104 (81%)	120 (72%)	
Shock requiring inotrope	Yes	18 (49%)	24 (19%)	42 (25%)	0.0004***
	No	19 (51%)	105 (81%)	124 (75%)	
Respiratory	Yes	19 (51%)	74 (57%)	93 (56%)	0.516
distress syndrome	No	18 (49%)	55 (43%)	73 (44%)	

^{***} highly significant

Regarding the risk factors leading to ROP, it was observed that birth asphyxia was present in 35 babies (21%) out of the total of 166 who were screened. ROP was identified in 8 babies (22%) with birth asphyxia and in 29 babies (78%) who did not have birth asphyxia. It was observed that the sepsis was present in 69 babies (42%) out of the total of 166 who were screened. ROP was detected in 28 babies (76%) with sepsis and in 9 (24%) babies who did not have sepsis. It was observed that blood transfusion was given in 46 babies (28%) out of the total of 166 who were screened for ROP. ROP was found in 21 babies (57%) who received transfusion and in 16 babies (43%) who were not given transfusion. It was found that shock requiring inotropes was present in 42 babies (25%) out of the total of 166 who were screened. ROP was present in 18 babies (49%) who had shock and in 19 babies (51%) who did not have shock. In this screening study of 166 babies, it was observed that respiratory distress syndrome (RDS) was present in 93 babies (56%). ROP was identified in 19 babies (51%) who had RDS and in 18 babies (49%) who did not have

RDS. Of the risk factors evaluated it was found that sepsis (p value <0.0001) and history of transfusion (p value 0.0001) and shock requiring inotropes (p value 0.0004) were statistically significantly associated with ROP (Table 2).

Regarding the mode of oxygen delivery as a risk factor for development of ROP it was found that when babies were administered oxygen by nasal prongs, 21 babies (61.8%) developed ROP while 13(38.2%) did not develop ROP. With use of hood to deliver oxygen, there were 22 babies (19.6%) who developed ROP and 90 (80.4%) did not develop ROP. With use of CPAP 17 (29.3%) developed ROP and 41(70.7%) did not have ROP. Among babies treated with mechanical ventilator, there were 5 babies (26.3%) developed ROP and 14(73.7%) did not. The odds of developing ROP was 12 times more in babies treated with prongs as compared to other modalities. OR (95%CI) 11.712 (4.921- 27.87). Administration of oxygen by nasal prongs was statistically significantly related to ROP (p value <0.0001) (Table 3).

Table 3: Association of different modes of O2 therapy among babies screened for ROP.

O2 modality	ROP	no ROP	Total	Chi square test p	Odds Ratio	95% C I	
O2 modality	(n=37)	(n=129)	1 Otal	value	Ouus Katio	Lower	Upper
Prongs	21	13	34	0.0001***	11.712	4.921	27.87
Other modalities	16	116	132	0.0001	11./12	4.921	21.01
Hood	22	90	112	0.769	0.636	0.298	1.354
Other modalities	15	39	54	0.709	0.030	0.298	1.334
CPAP	17	41	58	0.121	1.824	0.866	3.844
Other modalities	20	88	108	0.121	1.024	0.800	3.844
Ventilator	5	14	19	0.319	1.283	0.43	3.831
Other modalities	32	115	147	0.319	1.203	0.43	3.031

^{***}highly significant

Sepsis was observed significantly in more number 28 (76%) among those who had ROP when compared to 9 (24%) among those without ROP. The odds of having sepsis among babies with ROP is around 7 when compared to those without ROP [OR 6.67 (95% CI 2.89-15.43)].

Transfusion was observed significantly in more number 21(57%) among those who had ROP when compared to 16 (43%) among those without ROP. The odds of having received transfusion among babies with ROP is around 5 when compared to those without ROP [OR 5.46 (95% CI 2.49-11.95)].

Table 4: Risk factors for ROP.

	ROP						
Risk factor	Yes	No	Odds ratio	95	% C I	p value	
	(n=37)	(n=129)					
Sepsis-Yes	28	41	6.678	2.890	15.429	0.0001***	
Sepsis-No	9	88	0.078		13.429	0.0001	
Transfusion-Yes	21	25	5.460	2.405	11.051	0.0001***	
Transfusion-No	16	104	3.400	2.495	11.951	0.0001	
Shock requiring	18	24		1.895			
Inotrope-Yes	10	24	4.145		9.064	0.0001***	
Shock requiring	19	105	4.143		3.00 4	0.0001	
inotrope-No	19	103					

^{***}highly significant

Shock requiring inotropes was observed significantly in more number 18(49%) among those who had ROP when compared to 19 (51%) among those without ROP. The odds of having shock requiring inotropes among babies with ROP is around 4 when compared to those without ROP [OR 4.145 (95% CI 1.89-9.06)] (Table 4).

DISCUSSION

In present study retinopathy of prematurity (ROP) was detected in 22.3 % of neonates. In a study done by Chen YI et al retinopathy of prematurity was detected in 10.8% of neonates. However other studies have found a higher incidence of ROP. Of these studies done by Hungi BI et al found that the overall incidence of ROP was 41.5% and treatable ROP was 26.4% (24/91) of eyes diagnosed with ROP and 10.2% (24/236) of the overall eyes screened. In a study conducted by Pandhi et al where they screened 2240 babies and found that 33.2% had ROP.

The mean birth weight of babies with and without ROP identified in present study was 1480 grams and 1620 grams respectively. The mean gestational age of babies with and without ROP identified in present study was 32 weeks and 33 weeks respectively. This was similar to the observations made in other studies in that the mean birth weight and gestational age were lower in babies with ROP than in those without. Studies by Hungi BI et al and Mahuya Pal Chattopadhyay et al have also supported this. ^{8,10} Hungi BI et al in their study found that the mean birth weight and gestational age were lower in babies with ROP than in those without. ⁸ Hungi BI et al in their study found that the overall infants screened, 68 (57.6%) were heavier and older than the American screening cutoff. Of these, 36.8% had some stage ROP and 8%

required treatment.8 Mahuya Pal Chattopadhyay et al in their study found that the mean (SD) birth weight and gestational age of the neonates with and without ROP were 1410 (350) g and 31.8 (2.1) weeks; and 1820 (440) g and 32.9 (2.1) weeks, respectively. ¹⁰ In a study done by Pandhi et al it was observed that the mean gestational age of the babies with ROP was 30.7 (range: 23 to 37 weeks) and the mean birth weight was 1315.09 g (range: 650-2500 g). Among the babies with ROP, 31.9% had a birth weight more than 1500 g, the limit set by American Academy of Pediatrics. Observations by Parag K shah et al in their study support the fact that bigger, healthier and more mature babies presented with severe ROP than is currently the case in industrialized countries. 11 Similar observations were made by Sourabh Dutta and his team who stated that ROP blindness is not only occurring in very premature babies but also in heavier and more mature babies.12

In present study the risk factors for ROP were sepsis, blood transfusion and shock requiring inotropic support. Sepsis, transfusion and shock requiring inotropes individually and statistical significantly contributed to the risk of ROP with almost 7 times, 5 times and 4 times respectively. The incidence of ROP was 51% in babies with RDS while it was 49% in babies without RDS. In a study done by Chen YI et al the risk factors identified were low birth weight, apnoea >20 sec, anemia,placental abruption. 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.

Mahuya Pal Chattopadhyay et al in their study found that in univariate analysis, spontaneous vaginal delivery, nonadministration of antenatal steroids to mothers and apnea

were associated with the development of ROP. 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. 10 Study done by Chaudhari S et al found that the risk factors predisposing to ROP were septicemia, apnea, oxygen therapy and use of blood products.¹³ 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. 14 Birth weight and respiratory distress syndrome were independent risk factors in the development of mild ROP and birth weight in the development of severe ROP according to the study by Akkoyun I et al.15 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.16

CONCLUSION

ROP was more common in babies <34 weeks and in babies with birth weight <1750 grams. The mean birth weight of babies with and without ROP identified in present study was 1480 grams and 1620 grams respectively. The mean gestational age of babies with and without ROP identified in present study was 32 weeks and 33 weeks respectively. Sepsis, transfusion and shock requiring inotropes statistically significantly contributed to the risk of ROP. Analysis of the mode of oxygen therapy showed that use of prongs significantly increased the risk of ROP.

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