Original research article

Retinopathy of Prematurity Incidence and Risk factors in low-birth-weight Neonates Admitted in SNCU

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Abstract

Background: Retinopathy of prematurity (ROP) affects the developing retinal vasculature in premature neonates and is a complex condition. It typically happens in neonates who have undergone critical care, particularly those who have received prolonged oxygen therapy and those who have numerous other risk factors. the current study evaluated the incidence of ROP in preterm infants with a gestational age of fewer than 36 weeks of gestational age or a birth weight of less than 2000 gm admitted to SNCU.

Methods: This cross-sectional study was conducted at SNCU of Kakatiya Medical College and MGM Hospital, Warangal. ROP screening examinations can have short-term effects on blood pressure, heart rate, and respiratory function in the premature baby, examinations were kept as short as possible and precautions are taken to ensure that emergencies were dealt with promptly and effectively. The discomfort to the baby was minimized by pre-treatment of the eyes with a topical Proparacaine and swaddling the baby. Babies were fed at least one hour before the examination to avoid vomiting and aspiration.

Results: A total of n=102 babies were screened for the Incidence of Retinopathy of Prematurity (ROP) Overall incidence of ROP in the study was n=32(31.4%) the female to male ratio is 1.6:1. Out of the n=32 babies with ROP n=11 babies had stage 1 disease, n=13 babies had stage 2, n=5 babies had stage 3 disease, and n=2 babies had stage 4 disease. Out of n=32 babies, ROP positive cases n=2 babies had the disease in zone 1, n=2 babies had the disease in zone 1 & 2, n=6 babies had the disease in zone 2, n=10 babies had the disease in zone 2 & 3, n=12 babies had the disease in zone 3.

Conclusion: The incidence of ROP in the current study was found to be 31.4% and 40.63% of these cases were in the stage 2 ROP. The gestational age of neonates in the current study was taken to less than 36 weeks because low gestational age is an independent risk factor for ROP. On univariate analysis, the duration of oxygen administration, clinical sepsis, apnoea, RDS,

ventilation history, CPAP duration, neonatal jaundice, NEC, and hypotension are significantly associated with ROP.

Keywords: Retinopathy of Prematurity (ROP), Low birth weight babies, Oxygen therapy

Introduction

A Vaso-proliferative condition of the retina, retinopathy of prematurity (ROP), formerly known as retrolental fibroplasia (RFL), affects the retina. This condition is more likely to affect preterm infants, especially low birth weight (LBW) neonates who are exposed to a lot of oxygen (O_2). It is the main factor in neonatal blindness that is avoidable. [1] Early screening can lower the incidence of ROP and referral for treatment, according to the World Health Organization (WHO) program of Vision 2020 targeted against ROP. [2] The ROP spectrum is wide and includes sequelae that could endanger vision as well as a stage where it is recovering on its own. The incidence of ROP is 82 percent and the risk of blindness is 9.3 percent in infants with birth weights (BW) less than 1 Kg. [3] Due to inadequate screening, reporting, and education regarding the serious effects of the disease, there was initially a low incidence of ROP in underdeveloped nations like India. With improved screening procedures, wider access to assisted ventilation services, and higher preterm infant survival rates in newborn units, the incidence of preterm births appears to be rising. [4] The pathogenic mechanism underlying the development of ROP is multifactorial. [5] The risk of blindness is linked to several potential risk factors, including prematurity, hyperoxia, sepsis, necrotizing enterocolitis, intraventricular hemorrhage (IVH), low birth weight (LBW), prolonged exposure to oxygen (O_2), the severity of neonatal illnesses, severe respiratory distress requiring mechanical ventilation, shock, hypoxia, prolonged ventilatory support, need for blood transfusions, acidosis, anemia, high ambient light, and vitamin E deficiency. whereas breastfeeding was proposed to be having a protective effect. [5, 6] With this background we in the current study evaluated the incidence of ROP in preterm infants with a gestational age of fewer than 36 weeks of gestational age or a birth weight of less than 2000 gm admitted to SNCU of the pediatrics department, attached to Kakatiya Medical College, Warangal.

Material and methods

This cross-sectional study was conducted in the NICU of the Paediatric Department of MGM Hospital attached to Kakatiya Medical College Warangal, Telangana State from November 2019 to October 2021. Informed consent of parents was taken after explaining in detail the methods and procedures involved in the study in their language. Institutional Ethical Committee Clearance was taken before the study was obtained.

Inclusion Criteria

Preterm babies with GA of less than <or = 36wks and BW of less than 2000gm were delivered in (inborn babies) or referred (outborn babies) to the NICU of the pediatric department of MGM Hospital.

Exclusion Criteria

1. Children with major congenital malformations.
2. Children with suspected chromosomal anomalies.
3. Term babies.
4. Parents who have not given consent.

As soon as the baby fulfilling the inclusion criteria was admitted to NICU, the details were entered in a predesigned and structured proforma, which includes an assessment of the risk

factors. Informed consent was taken from the parents and baseline data were collected for each baby regarding date of birth, sex, single or multiple births, intrauterine growth retardation, and other antenatal insults. During the stay, heart rate, blood pressure, monitoring for apnoea monitoring and O_2 saturation was done by continuous pulse oximetry. Clinical assessments and lab investigations for identifying the risk factors were done.

Preparation and precautions: All the precautions were taken. Since ROP screening examinations can have short-term effects on blood pressure, heart rate, and respiratory function in a premature baby, examinations were kept as short as possible and precautions are taken to ensure that emergencies were dealt with promptly and effectively. Eye examination during screening lasts several minutes and may cause considerable pain to the neonate. Discomfort to the baby was minimized by pre-treatment of the eyes with a topical Proparacaine and swaddling the baby. Babies were fed at least one hour before the examination to avoid vomiting and aspiration. Hand washing was done and asepsis was maintained.

Dilatation of the pupil: Pupils were dilated with Phenylephrine 2.5% and Tropicamide 0.5%. One drop of Tropicamide was instilled every 10-15 minutes 4 times starting 1 hour before the scheduled time for examination. This was followed by Phenylephrine, one drop just before the examination. Phenylephrine, which is available in 10% concentration, was diluted 4 times before use in neonates. Repeated instillation of Phenylephrine was avoided for the fear of hypertension.

*Screening***:** Screening of ROP was done with Retcam Shuttle (Clarity MSI, USA) by an experienced ophthalmologist in our NICU. After instilling a topical anesthetic drop like Proparacaine, a wire speculum was inserted to keep the eyelids apart. First, the anterior segment of the eye was examined to look for tunica vasculosa lentis, pupillary dilation, and lens/media clarity; followed by the posterior pole to look for plus disease; followed by a sequential examination of all clock hours of the peripheral retina. A scleral depressor was used to indent the eye externally to examine areas of interest and rotate and stabilize the eye. Notes were made after each ROP examination, detailing zone, stage, and extent in terms of clock hours of any ROP and the presence of any pre-plus or plus disease. These notes included a recommendation for the timing of the next examination and were kept with the medical record. After screening, the cases were classified as per ICROP based on vascularization of the retina and characterized by its position (zone), and severity (stage).

Statistical methods: Data was entered into Microsoft Excel and analyses were done using the Statistical Package for Social Sciences (SPSS) for Windows software (version 22.0; SPSS Inc, Chicago). Descriptive statistics such as mean and standard deviation (SD) for continuous variables, frequencies, and percentages were calculated for categorical variables were determined. Association between variables was analyzed by using the Chi-Square test for categorical Variables. Unpaired t-test was used to compare the mean of quantitative variables 30 between simple and complex seizures. Bar charts and Pie charts were used for the visual representation of the analyzed data. The level of significance was set at ($p<0.05$).

Results

A total of n=102 babies were screened for the Incidence of Retinopathy of Prematurity (ROP) Overall incidence of ROP in the study was n=32(31.4%) the female to male ratio is 1.6:1. No statistical significance was noted between the gender and ROP incidence details depicted in table 1.

Table 1: The distribution of cases included in the study

Gender	*ROP*		*Total*
	Present (n=32)	*Absent (n=70)*	
Male	20 (39.2)	31 (60.8)	51
Female	12 (23.5)	39 (76.5)	51
Total	32	70	103
Chi-square test p-value = 0.99 (Not Significant)			

Out of the n=32 babies with ROP n=11 babies had stage 1 disease, n=13 babies had stage 2, n=5 babies had stage 3 disease, and n=2 babies had stage 4 disease details depicted in figure 1. Out of n=32 babies, ROP positive cases n=2 babies had the disease in zone 1, n=2 babies had the disease in zone 1 & 2, n=6 babies had the disease in zone 2, n=10 babies had the disease in zone 2 & 3, n=12 babies had the disease in zone 3.

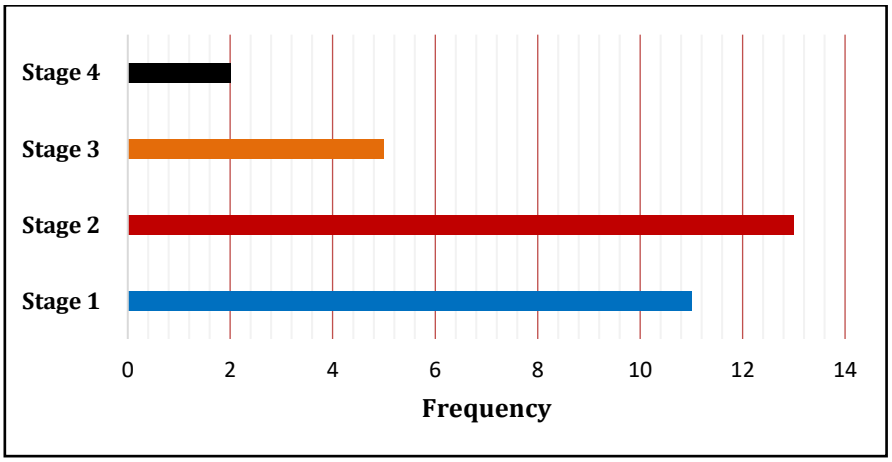

Figure 1: showing the distribution of cases in various stages of ROP

In less than <1200gm weight babies n=17 (73.9%) cases screened were positive for ROP, in 1200-1600gm weight babies n=43(20%) screened were positive, in 1600- 2000gm weight babies n=36(16.7%) screened were positive for ROP the p-Value was found to be <0.001, hence it is Significant. This shows that lower birth weight is considered a significant risk factor for the development of ROP. The incidence of ROP in babies who received oxygen for <5 days is 9.5%, in 6-10 days 40%, in 11-15 days 42.1%, in 16-20 days 53.85, and in >20 days 50%. As the duration of oxygen exposure increases the incidence of ROP significantly increases given in table 2.

Table 2: The duration of oxygen therapy and ROP

O_2 Duration days	ROP		Total
	Present	Absent	
< 5 days	2	19	21
6 – 10	10	15	25
11 – 15	8	11	19
16 – 20	7	6	13
> 20 days	3	3	6
Total	30	54	84
Chi-square test p-value <0.05 (significant)			

The incidence of ROP in neonates who received CPAP for <4 days is n=8(27.6%) out of the total n=29 who received CPAP, and in those who received for >4 days n=19(59.4%) out of total n=32 cases who received CPAP for >4 days. 61.5% of neonates with a history of ventilation had developed the ROP changes, and 27% of neonates with absent ventilation history developed the ROP changes. Therefore, there is a significant association noted between the ventilation history and incidence of ROP depicted in table 3.

Table 3: Ventilation History and ROP

Ventilation History	ROP		Total
	Present (n=32) n (%)	Absent (n=70) n (%)	
Yes	8 (61.5)	5 (38.5)	13
No	24 (27.0)	65 (73.0)	89
Chi-Square Test, P Value = 0.012, Significant			

All the cases of ROP n=32 were also associated with clinical sepsis. Out of n=34 cases with neonatal hyperbilirubinemia n=19 (55.9%) developed ROP changes the P-Value <0.001, hence Significant. Out of n=32 neonates n=17 (53.1%) neonates with history of shock developed the ROP changes the P-Value = 0.001, Significant. In our study overall n=11 neonates developed *Necrotizing enterocolitis* (*NEC*) in those n=7 neonates (63.6%) developed the ROP changes. In this study group, n=20 neonates have anemia in those n=11 babies (55%) who developed the changes of ROP. Out of n=53 neonates who developed respiratory distress syndrome (RDS) n= 25 (47.2%) were with ROP the p-value was 0.05 and significant. No association was noted between the history of Resuscitation and the incidence of ROP. No protective effect was found between antenatal steroids and the incidence of ROP. There is no significant association noted between the usage of drugs in the mother and the incidence of ROP. Out of n=31 babies who are, having a history of hypothermia, n=13 babies (41.9%) developed ROP changes. p-value shows not significant. In our study, no significant association was noted between the low APGAR scores and the incidence of ROP.

Discussion

Retinopathy of prematurity ROP screening is important because it can help avoid childhood blindness, which is ROP's most prevalent cause. Limiting exposure to prenatal, natal, and postnatal risk factors which are hypothesized to contribute to both the increased incidence and severity of ROP can be done to avoid ROP in its primary forms. Early diagnosis and treatment can avoid blindness in people with severe ROP who are screened but not treated. Early screening prevents secondary ROP. As a result, the WHO Vision 2020 initiative places a high priority on secondary prevention of ROP. [2] ROP is becoming a major issue in emerging nations like India in this era of rising neonatal care standards. Although there are data from various urban and rural locations of India, there aren't any reports from sizable randomized multicentric trials conducted here. Therefore, information on the epidemiology of ROP from the Indian subcontinent is scarce. Although the clinical spectrum and incidence of ROP are not the same in all units, studies from developed nations have shown that there is a general decline in the occurrence of the condition wherever there is an ongoing surveillance program. Therefore, prompt screening is a crucial component of ROP care. The incidence of ROP in the current study was 31.4% Verma et al., [7] in a similar study found the incidence of ROP at 23.4% however they have taken Birth weight < 1500 gms. Nair et al., [8] found the incidence

of ROP at 25.4% with a cut-off birth weight of < 1500 gms. Studies in the literature usually use a cut-off point of a BW of 1250 gms or 1500gm or 1750gm, a GA of 28 weeks or 32 weeks, or both. Using a BW of 2000 gms or less, a GA of 36 weeks or less, or both as criteria for inclusion in this study explains the higher incidence of ROP when compared to other Indian studies. Patil et al., [9] reported the overall incidence of ROP as 17.5% and there was no case of severe ROP they studied 40 babies with <32 weeks or < 1250 gm. Maheshwari et al., [10] reported overall incidence as 20% and severe ROP as 7%. They studied 66 babies with <35wk or < 1500 gm. Gupta et al., [11] reported overall incidence as 21.7% and severe ROP as 5% they studied n=60 babies with ≤ 35 weeks or ≤1500gm. Dutta et al., [12] screened n=108 babies of ≤32 weeks or ≤1700 gm and reported an overall incidence of 21%. Though accumulating evidence indicates that ROP is a multifactorial disease, immaturity of the retina and a period of hyperoxia are the main contributing etiological factors in the pathophysiology of ROP. On univariate analysis, birth weight, gestational age, the duration of oxygen administration, clinical sepsis, neonatal hyperbilirubinemia, apnoea, RDS, administration of blood and its products, and hypotension are significantly associated with the development of ROP. However, in most instances, it is not possible to compare studies, as the inclusion criteria are different. The prevalence of ROP was more among very low birth weight neonates and the risk is inversely proportional to BW and GA in studies conducted by Maheshwari et al., [10] Incidence and severity of ROP increased as the birth weight decreased.

The duration of oxygen administered was an independent risk factor for the development of ROP ($p<0.05$). 68.6% of babies who received oxygen therapy developed ROP in the present study and nearly 50% of the babies on oxygen therapy developed the disease in other studies like in Verma N et al., [7] study 59.7% of babies who received oxygen therapy developed the ROP changes. Respiratory distress syndrome is a significant risk factor in the present study. Gupta et al14 and associates reported ROP in 33.3% of babies with RDS. In Verma N et al., [7] study 20.83% of babies with RDS developed the ROP. In our study, 47.2% of babies in cases had RDS, which is almost comparable to the other studies mentioned. Clinical Sepsis is a risk factor for ROP in the present study ($p<0.001$) and corroborates with findings of other studies. Gupta et al., [11] in their study reported that 52% of the babies with clinical sepsis had the ROP changes. In Verma N et al., [7] study 26.38% of neonates with ROP changes had clinical sepsis. In the present study, clinical sepsis was a risk factor in univariate analysis and 53.3% of the cases had clinical sepsis. ROP is known to be associated with apnea. This can be compared to 54.1%, 54.5%, and 38.8% as reported by Gupta et al., [11] and Verma N et al., [7] respectively, in our study group 50.0% of neonates with a history of apnea developed the ROP changes. Apnea was also found to be a risk factor for ROP in studies conducted by Shohat et al., [13] and Gunn et al., [14] In the present study, mechanical ventilation was required for n=13 babies in those 8 babies (61.5%) developed the ROP changes. In a study conducted by Verma N et al., [7] 43.5% of the neonates with a history of ventilation developed ROP changes. Ventilation history is considered a significant risk factor for the development of ROP in our study.

Conclusion

The incidence of ROP in the current study was found to be 31.4% and 40.63% of these cases were in the stage 2 ROP. The gestational age of neonates in the current study was taken to less than 36 weeks because low gestational age is an independent risk factor for ROP. On univariate analysis, the duration of oxygen administration, clinical sepsis, apnoea, RDS, ventilation history, CPAP duration, neonatal jaundice, NEC, and hypotension are significantly associated with ROP. No association of ROP with other factors like PIH, PROM, history of antenatal steroids, and history of drug usage in the mother during the antenatal period.

References

1. Isenberg SJ. Eye disorders. In MacDonald MG, Mullet MD, Seshia MMK, editors. Avery's Neonatology-Pathophysiology and Management of the Newborn. 6th ed. Philadelphia, PA: Lippincott Williams and Wilkins; p.1469-84.
2. Gilbert C, Foster A. Childhood blindness in the context of vision 2020 the right to sight. WHO Bulletin 2001; 79:227-32.
3. Palmer EA, Flynn JT, Hardy RJ, Phelps DL, Phillips CL, Schaffer DB, Tung B. Cryotherapy for Retinopathy of Prematurity Cooperative Group. Incidence and Early Course of Retinopathy of Prematurity. Ophthalmology. 2020; 127(4S): S84-S96.
4. The Cryotherapy for Retinopathy of Prematurity Cooperative Group. Incidence and early course of retinopathy of prematurity. Ophthalmology 1991 Nov; 98(11):1628-40.
5. Chawla D, Agarwal R, Deorari AK, Paul VK. Retinopathy of prematurity. Indian J Pediatr 2008; 75(1):73-76.
6. Vanderveen DK, Zupancic JAF. Retinopathy of Prematurity. In: Cloherty JP, Eichenwald EC, Stark AR, editors. Manual of neonatal care. 6th ed. Philadelphia, PA: Lippincott Williams and Wilkins; 2010. p.640-44.
7. Verma A, Nema N, Patel S, Ishrat S, Sidharth M. Retinopathy of prematurity: incidence and risk factors. Int J Ophthalmol Eye Sci. 2016; 4:198-201.
8. Nair P, Ganesh A, Mitra S, Sham S, Ganguly. Retinopathy of Prematurity in VLBW and extreme LBW babies. Indian J Paediatrics 2003;70(4):303-06.
9. Patil J, Deodhar J, Wagh S, Pandit AN. High-risk factors for the development of Retinopathy of Prematurity. Indian Pediatrics 1997; 34:1024-7.
10. Maheshwari R, Kumar H, Paul VK. Incidence and risk factors of retinopathy of prematurity in a tertiary care newborn unit in New Delhi. Natl Med J India 1996; 9:211-4.
11. Gupta VP, Dhaliwal U, Sharma R, Gupta P, Rohatgi J. Retinopathy of prematurity–risk factors. Indian J Pediatr 2004; 71:887-92.
12. Narang A, Dutta S, Dogra M, Gupta A. Risk factors of threshold retinopathy prematurity. Indian Pediatrics 2003; 41:665-70.
13. Shohat M, Reisner SH, Krikler R, Nissenkorn I, Yasser Y, Ben-Sira I. Retinopathy of Prematurity: Incidence and Risk Factors. Pediatrics 1983; 72(2):159-63.
14. Gunn TR, Easdown J, Outerbridge EW. Risk factors in Retrolental Fibroplasia. Pediatrics 1980; 65:1096.