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Original Research Article

Incidence and Risk Factor Profile of Retinopathy of Prematurity at a Tertiary Care Centre

Ch Stephen[1], Vannala Raju[2], Sreenivasa K Rao[3], Narayana Lunavath[2]

[1]Junior Resident, Department of Paediatrics, ESI Medical College Hospital and Super Speciality Hospital, Hyderabad, Telangana,
[2]Assistant Professor, ESI Medical College Hospital and Super Speciality Hospital, Hyderabad, Telangana
[3]Associate Professor, Department of Pediatrics, ESI Medical College Hospital and Super Speciality Hospital, Hyderabad, Telangana

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Corresponding Author: Dr Narayana Lunavath
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Abstract:
Retinopathy of prematurity is a vaso-proliferative disorder of the retina. Preterm infants are more prone for this disease especially low birth weight (LBW) neonates who are exposed to large amount of oxygen(O2). It is the leading cause of the preventable blindness in infants. This study was conducted to find the incidence of ROP in this region and to study the contribution of different risk factor profile to ROP. The study is a descriptive and observational study. A total of 400 preterm neonates satisfying the inclusion criteria were included in the study. The incidence of ROP was 10.25%. The duration of oxygen administration, need for oxygen supplementation, clinical sepsis, apnea, RDS, HIE, acute kidney injury, convulsions, positive CRP, administration of blood and its products and hypotension were significantly associated with development of ROP.
Keywords: ROP, Prematurity, Oxygen Therapy, Retinopathy.

Introduction

Retinopathy of prematurity (ROP), whichwas previously called as Retrolental Fibroplasia (RFL), is a Vaso-proliferative disorder of the retina. Preterm infants are more prone for this disease especially low birth weight (LBW) neonates who are exposed to large amount of oxygen (O2). It is the major cause of preventable blindness in children [1].

The World Health Organization (WHO) programme of Vision 2020 targeted against ROP mentioned that the incidence of ROP can be reduced by early screening and referral for treatment [2]. Spectrum of ROP is broad and ranges from a spontaneously recovering stage to a vision threatening sequelae. In infants with birth weight (BW) less than 1000grams, the risk of ROP is 82% and 9.3% of them are potentially under the risk of blindness [3]. There is an apparently increasing incidence with better screening protocols, more availability of assisted ventilation services and increased survival of preterm in newborn units [4]. The pathogenic process involved in causation of ROP is multifactorial [5]. It is attributed to many possible risk factors like prematurity, hyperoxia, sepsis, necrotizing enterocolitis, intraventricular hemorrhage(IVH), low birth weight (LBW), prolonged exposure to O_2, severity of neonatal illnesses, severe respiratory distress requiring mechanical ventilation, shock, hypoxia, prolonged ventilatory support, need for blood transfusion, acidosis, anemia [5,6]. In recent times, neonatal care has improved a lot in respect of preterm babies, monitoring of O_2 therapy and awareness of ROP as well as management of various risk factors of ROP. Hence, this study was conductedto find the incidence of ROP and to study the contribution of different risk factors to ROP.

Study Objective

- To determine the incidence of Retinopathy of Prematurity in all neonates less than 34 weeks of gestation age registered in NICU.
- To assess the risk factor profile associated with Retinopathy of Prematurity.

Methods and Methodology

This prospective observational study conducted at our tertiary care center, ESIC medical college hospital, Sanath Nagar, Hyderabad during a period of six months. 400 babies were studied.

Inclusion Criteria

- Preterm babies with GA of less than 34wk delivered in or referred to the NICU of ESIC Medical college and Hospital, Hyderabad.
- BW of less than 1800gm

Exclusion Criteria

- Babies with GA >34 wks
- Babies with BW >1800grams (gm).
- Refusal of consent.

The details were entered in a predesigned proforma which includes 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 apnea and O_2 saturation was done by pulse oximetry. Clinical assessments and lab investigations for identifying the risk factors like apnea, prematurity, respiratory distress syndrome (RDS), oxygen therapy, sepsis. RDS, surfactant administration, necrotizing enterocolitis (NEC), apnea of prematurity, pulmonary hemorrhage, patent ductus arteriosus (PDA), hypoxic ischemic encephalopathy (HIE) and intraventricular hemorrhage (IVH) were considered as severe illnesses for the study.

Screening of ROP was done with Retcam Shuttle (Clarity MSI, USA) by an experienced ophthalmologist in our NICU. 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. Afterscreening, the cases were classified as per ICROP on the basis of vascularization of the retina and characterized by its position (zone), severity (stage), and extent (clock hours). Follow up was done as recommended by the ICROP.

Results

400 babies fulfilling the inclusion criteria were screened. Neonates who developed any stage of ROP were considered as cases and the neonates without ROP were considered as controls. Overall incidence of ROP among study group was 10.25% (41 babies) out of them 39 were stage 1 ROP, and 2 were stage 2 ROP. Table no.1 shows different parameters related to birth details. Majority of the cases (63.41%) were in gestational age between 29weeks and 32 weeks and most of the controls (83.84%) belonged to 32 to 34 weeks gestational age. Preterm gestational agewas significantly associated with ROP (p<0.0001). ROP was seen more in male babies when compared to female babies. Incidence was more in vaginally delivered babies but there was no statistically significant difference in sex distribution and mode of delivery among cases and controls. Maximum number of cases (58.53%) had birth weight ranging between 1501 to 1800 gm. Low birth weight was significantly associated with increase of ROP (P value <0.0001). Among the birth details preterm gestational age and low birth weight were found to increase the risk of ROP.

Other risk factors profile studied included antenatal and neonatal risk factors (table no.2). Antenatal factors like maternal pregnancy induced hypertension (PIH), antenatal steroids administration, meconium-stained liquor (MSL), antepartum haemorrhage (APH) was not found to increase the risk of ROP. Some of the neonatal factors like need ofoxygen therapy, apnea, need of resuscitation, presence of signs of clinical sepsis, hypoxic ischemicencephalopathy (HIE), acute kidney injury (AKI), neonatal seizures, hypotension was found more in cases then in controls which were statistically significant (p<0.0001). Anemia, blood transfusionhistory, neonatal jaundice, patent ductus arteriosus (PDA), intraventricular hemorrhage (IVH), necrotizingenterocolitis (NEC), hemolytic disease of newborn (HDN), hypothermia was not found to be associated with ROP.

Table 1: Birth details

Birth details		Cases (n=41)	Controls(n=359)	P value
Gestational	<28WK	2	8	<0.0001
age		(4.87%)	(2.22%)	
	29 TO	26	50	
	32 WK	(63.41%)	(13.92%)	
	32 TO	13	301	
	34 WK	(31.70%)	(83.84%)	
Mode of	LSCS	10	73	0.6866
delivery		(24.93%)	(20.33%)	
	NVD	31	286	
		(75.60%)	(79.67%)	
Sex of the	Male	25	193	0.152
baby		(11.46%)	(88.53%)	
	Female	16	166	
		(9.87%)	(91.20%)	
Birth	<1000g	1	1	<0.0001
weight		(2.43%)	(0.27%)	
	1001 to	16	139	

	1500g	(39.02%)	(38.71%)	
	1501g	24	219	
	to	(58.53%)	(61%)	
	1800g			

Table 2: ROP associated risk factors

Associated Risk factors (Y-Yes, N-No)			Cases (n=41)	Controls (n=359)	P value
Antenatal factors	PIH	Y	9 (21.95%)	69 (19.22%)	0.6787
		N	32(78.04%)	290 (80.77%)	
	Antenatal steroid	Y	7 (17.07%)	53 (14.76%)	0.6322
		N	34 82.92%)	306 (85.23%)	
	MSL	Y	9 (21.95%)	82 (22.84%)	0.8975
		N	32 (78.04%)	277 (77.15%)	
	APH	Y	6 (14.63%)	70 (19.49%)	0.782
		N	35 (85.36%)	289 (80.50%)	
Neonatal factors	Need foroxygenation	Y	27 (65.85%)	85 (23.67%)	0.0001
		N	14 (34.14%)	274 (76.32%)	
	Clinical sepsis	Y	28 (68.29%)	165 (45.96%)	0.001
		N	13 (31.70%)	194 (54.03%)	
	HIE	Y	27(65.85%)	21 (23.39%)	0.0001
		N	14 (34.14%)	338 (76.60%)	
	AKI	Y	9(21.95%)	21 (5.84%)	0.0001
		N	32(78.04%)	338(94.15%)	
	Neonatal Seizures	Y	7(17.07%)	13(3.62%)	0.0001
		N	34 (82.92%)	346 (96.37%)	
	Hypotens ion	Y	13(31.70%)	44(12.25%)	0.0017
		N	28(68.29%)	315(87.74%)	
	Anaemia	Y	9(21.95%)	41(11.42%)	0.0925
		N	32(78.04%)	318(88.57%)	
	Jaundice	Y	27(65.85%)	177(49.30%)	0.0653
		N	14(34.14%)	182(50.69%)	
	PDA	Y	3(7.31%)	22(6.12%)	0.7324
		N	38(92.68%)	337(93.87%)	
	IVH	Y	2(4.87%)	4(1.11%)	0.12
		N	39(95.12%)	355(98.88%)	
	NEC	Y	0	9(2.50%)	0.6158
		N	41 (100%)	350 (69.63%)	
	HDN	Y	1 (2.43%)	25 (6.96%)	0.4990
		N	40 (97.56%)	334 (93.03%)	
	Hypoth ermia	Y	4 (9.75%)	28 (7.79%)	0.5553
		N	37 (90.24%)	331 (92.20%)	

There was significant (P<0.0001) increasein duration of hospital stay in cases of ROP. 60.97% of cases needed NICU stay for >13 days.

Discussion

Significance of ROP screening lies in the fact that ROP is the most common cause ofchildhood blindness which is preventable. Prevention of ROP by screening is given utmost importance in the WHO VISION 2020 programme [5]. The incidence of ROP in the present study is 10.25%. Various studies [6,7,8,9] showed incidence varying from 9.4%-25.4% in babies with gestational age 32wk or less develop some degree of ROP. Screening of babies with a GA of <34wk and/or <1800gm BW in this study has made the incidence of ROP comparable to other Indian studies.

Though accumulating evidence indicatesthat ROP is a multifactorial disease, immaturity of retina and a period of hyperoxia are the main contributing etiological factors in the pathophysiology of ROP [10]. In our study, the incidence of ROP was inversely proportional to both birth weight (p=0.0001) and gestational age (p< 0.0001) significantly. The prevalence of ROP was more among VLBW neonates and the risk isinversely proportional to BW and GA in a study conducted by Maheshwari et al [6]. The duration ofoxygen administered is a risk factor for development of ROP (p=0.0001). 65.85% 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 [8]. The causal link between ROP and supplemental oxygen has been confirmed by controlled trials and clinical studies [11,12]. However, a safe level of oxygen usage has not been defined. Preliminary work has suggested that continuous oxygen monitoring mayreduce the incidence of ROP. In present study oxygen administration is a significant risk factor for development of ROP and an independent risk factor on multivariate analysis. A study conducted by Higgins et al [13] showed that antenatal steroid administration by the mother had a protective effect against ROP in the neonates. But in our study, it was not a significant risk factor may be because the timing of steroid administration and delivery not considered in our study. RDS is significant risk factor in the present study but not an independent risk factor on multivariate analysis. Gupta et al [8] reported ROP in 33.3% of babies with RDS.

It has been hypothesized that the adult hemoglobin, being more capable of releasing oxygen to tissues, causes tissue-level hyperoxia and causeROP [14]. The hyperoxia in the tissues leads on to free oxygen radical release and reflex vasoconstriction leading on to the familiar cascade of events that causes ROP [15,16]. In our study blood transfusion was found to be a risk factor for development of ROP on univariate analysis, but not so on multivariate analysis. Exchange transfusion has been identified as a risk factor for the development of ROP by Rekha etal [17] and Maheshwari et al [6]. Clinical Sepsis is a risk factor for ROP in the present study (p=0.001) and corroborates with findings of other studies [12,17,18,19]. Inthe present study clinical sepsis was a risk factor on univariate analysis, but it was not an independent riskfactor on multivariate analysis. Its prevention andearly treatment may reduce the incidence of ROP. ROP is known to be associated with apnea [8,12,20]. In our study 51.21% cases has apnea. Apnea was a risk factor on univariate analysis and presence of apnea was an independent risk factor for ROP on multivariate analysis. This can be compared to 54.1%and 54.5% as reported by Agarwal [12] and Gupta [8] respectively. Apnea was also found to be risk factor for ROP in studies conducted by Shohat et al [21] and Gunn and co-workers [19].

On univariate analysis, the duration ofoxygen administration, need for oxygen supplementation, clinical sepsis, apnea, RDS, HIE, acute kidney injury, convulsions, positive CRP, administration of blood and its products and hypotension were significantly associated with development of ROP. On multivariate analysis,apnea, need for resuscitation and need for oxygen administration was found to be independently significant risk factors.

Conclusions

In this era of improving standards of neonatal care, ROP is becoming a significant problem in developing countries like India. ROP is one of the important preventable causes of childhood blindness. The primary prevention of ROP can be done by limiting the exposure to antenatal, natal and postnatal risk factors which are proposed to contribute to the increased incidence as well as severity of ROP. Secondary prevention of ROP is done by timely screening and early treatment to prevent blindness that can occur in severe ROP who miss the screening and are not treated.

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