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To Study the Prevalence and Risk Factors of Retinopathy of Prematurity at a Tertiary Care Centre in Agra

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Abstract: ***Aim: The aim of this study to estimate the prevalence of retinopathy of prematurity and to identify the risk factors which predispose to retinopathy of prematurity. Subjects and Method: The present prospective study was conducted at upgraded department of ophthalmology and department of paediatrics, Sarojini Naidu Medical College, Agra, India from November 2014 to October 2016. Neonates with gestational age <34 weeks and/or birth weight < 1750 g or 34-36 weeks gestational age and/or a birth weight between 1750-2000 g with additional risk factors were included in this study. Diagnosis of ROP was done by an indirect ophthalmoscopy at 4-6 weeks postnatal age. Result: Of the total 155 infants screened, ROP was seen in 35 infants with overall prevalence 22.58%. The prevalence of ROP was 25.6% among gestational age<32 weeks and 10% among gestational age > 32 weeks infants. The prevalence of ROP among <1000g, 1000-1500g, >1500-2500g and >2500g infants was 80%, 57.50%, 8.5% and 5%, respectively. Of the 155 babies screened, 20 (57.14%) were in stage 1, 10 (28.57%) were in stage 2, 5 (14.28%) were in stage 3. None of the studied neonates presented ROP at stages 4 and 5. Sepsis, intra ventricular haemorrhage, blood transfusion, oxygen therapy, twins delivery was found to be statistically significant for the development of retinopathy of prematurity. Conclusion: The prevalence of ROP among high risk babies is significant. The data of this study suggest that low gestational age, sepsis, oxygen therapy, frequency of blood transfusion, twins delivery are independent risk factors in the development of ROP. All high risk babies should be screened for ROP as early screening and intervention can help to increase the child's chances of better vision and hence better quality of life and also reduce the load of paediatric blindness due to ROP.***

Keywords:

1. Introduction

Retinopathy of prematurity (ROP) is a disorder of the developing retina of low birth weight preterm infants that potentially leads to blindness in a small but significant percentage of those infants. ROP is an important preventable cause of blindness in children[1]; it is believed to account for 6-18% of childhood blindness in developed countries[2]; and in India it accounts for 20%-40%. The most important determinant of any ROP management program is an effective screening. Early identification of retinal damage and institution of appropriate treatment prevent blindness and offer child better overall development. ROP is under epidemiological study around the world[3]; ROP is characterized by abnormal neo-vascular development in the retina of premature infants. Three factors have shown consistent and significant association of ROP; low gestational age, low birth weight and prolonged exposure to supplementary oxygen following delivery[4,5,6]; Other putative risk factors include mechanical ventilation[7]; sepsis[8]; intra ventricular haemorrhage[9]; surfactant therapy[9]; anaemia[10]; frequent blood transfusions[10]; and apnoea[7]. The precise role of these factors individually in the progression of the disease have not yet been determined[11]; Our study estimated the status of ROP in our tertiary centre so that these data will help to make further strategies to prevent blindness due to ROP.

2. Material and Methods

The present prospective observational study was conducted at Ophthalmology department in cooperation with department of Paediatrics of tertiary care centre in Agra, India from November 2014 to October 2016. Ethical clearance was obtained from hospital ethics committee and informed consent of parents was also obtained. 155 preterm infants admitted to the neonatal intensive care unit or discharged with gestational age <34 weeks and/or birth weight <1750g or gestational age 34-36 weeks and/or birth weight between 1750-2000g with any of the risk factors (mechanical ventilation, prolonged oxygen therapy, hemodynamic instability, blood transfusion, sepsis, patients on phototherapy, intra ventricular haemorrhage, history of twins delivery, history of HIE, history of maternal vaginal leakage) were included in the study. Infants with congenital anomalies, chromosomal abnormalities, and inborn errors of metabolism were excluded from the study. Examination of the eye was done in the NICU or in the neonatal follow up clinic at 4-6 weeks postnatal age. All the screened babies (ROP and non ROP) were followed weekly or biweekly up to complete maturation of peripheral retina or until full remission of ROP after treatment. Diagnosis of retinopathy of prematurity was done by binocular indirect ophthalmoscopy with 20D lens. Eyes were examined with an infant speculum and a scleral depressor under topical anaesthesia using 2% proparacaine drops. The pupils were dilated by using 0.4% tropicamide + 1.25% phenylephrine eye drops two or three times, till full dilatation occurred. ROP was graded into stages and zones as per the international classification of ROP.

3. Results

Total 155 infants were screened for ROP. There were 90 males (58%), and 65 females (41.9%).Mean gestational age 30.54 ± 1.04 weeks; 120 were <32 weeks and 35 were >32

weeks. The mean birth weight was 1880 ± 642 g. 100 cases (64.5%) were delivered vaginally and 55 cases (35.5%) were delivered by caesarean section. Of 155 babies 80 belongs to urban area and 75 belong to semiurban/ rural areas

Out of 155 infants; 35 (22.58%) cases developed ROP in one or both eyes classified as 20 (57.14%) cases stage 1, 10 (28.57%) cases stage 2, and 5 (14.28%) cases stage 3. None of the studied infants presented ROP at stage 4 and 5. Out of 35 infants 19 were male and 16 were female.

Demographic profile and risk factors of ROP has been described in table 1

There was significant relationship between occurrence of ROP and gestational age (p=0.036), low birth weight (p=0.001), sepsis (p=0.003), IVH (P=0.0001), blood transfusion (p<0.0001), oxygen therapy (p=0.0126), h/o twins (p=<0.0001). On the other hand there was no significant relationship between the occurrence of ROP and sex, mode of delivery, respiratory distress syndrome, IVH, phototherapy, mechanical ventilation, CRP positive, and HIE (all p>0.05).

4. Discussion

Retinopathy of prematurity is a disorder of retinal vascular development in preterm babies. It continues to be a significant complication in preterm neonates despite advances in neonatal care and remains a major cause of childhood blindness worldwide[12]. The prevalence of ROP in this study was 22.58% and this was comparable to some other studies in India[13] and Singapore[7]. ROP is a multifactorial disease involving many factors. Low gestational age, low birth weight, sepsis, oxygen therapy, respiratory distress syndrome, and blood transfusion have been suspected to influence the incidence of ROP[14]. The most significant risk factors for development of ROP were low gestational age and low birth weight, as shown in many studies[6, 11, 15]. In our study, low gestational age, sepsis, oxygen therapy, frequency of blood transfusions, maternal vaginal leakage more than two days and history of twins were found to be risk factors for development of ROP independently. Meanwhile, sex, mode of delivery, respiratory distress syndrome, phototherapy, duration of oxygen therapy, mechanical ventilation, vaginal leakage for less than two days , CRP positive were non- significant risk factors by using univariate analysis. As regard the effect of low gestational age on occurrence of ROP, we found it is the most important risk factor in ROP. This was in agreement with the results of studies done by Shah *et al.*[7], Karna*et al.*[9], and Fortes *et al.*[16]. This was explained by immaturity of vascularization that induces an increased susceptibility of the retina to oxidative damage and to a number of perinatal factors which include hyper and hypoxia, blood transfusions and sepsis. We found that low birth weight was significant factor for development of ROP. This was supported by many studies[7, 18, 17] which reported that lower birth weight was significantly associated with development of ROP, and explained that by more susceptibility for oxygen therapy, prolonged ventilation, sepsis, and blood transfusions in very low birth weight infants. In this study, we found that sepsis was significantly associated with the development of ROP. This was in agreement with Shah *et al.*[7], and Vinekar*et al.*[18], which may be due to effect of endotoxins on retinal blood vessels. Oxygen therapy was an independent risk factor for the development of ROP[7, 13,] . We found a significant relationship between the occurrence of ROP and use of oxygen therapy, but there was no significant relationship between oxygen therapy and stages of ROP.In our study, we foundit insignificant which was in agreement with the result of Dutta*et al.*[19]Though some studies reported that duration of oxygen therapy more than 7 days was a significant risk factor for development of ROP[7, 20].In our study, we found that the frequency of blood transfusions is an independent risk factor for development of ROP. This can be explained by the fact that, adult RBCs are rich in 2, 3 DPG and adult haemoglobin which binds less firmly to oxygen, thus releasing excess oxygen to the retinal tissue. While Hirano *et al.*[21] stated that it is controversial and iron overload rather than number of transfusions may contribute to the development of ROP. Other risk factors including respiratory distress syndrome, CRP positive and phototherapy showed insignificant relationship with the occurrence of ROP. Similarly Taqui*et al.*[22], reported insignificant relation between ROP and patent ductusarteriosus and intra-ventricular haemorrhage, but observed a significant relation between respiratory distress syndrome and the development of ROP and related this to the fact that systemic hypoxia results in retinal hypoxia and more need for oxygen therapy. On the other hand, Shah *et al.*[7] reported a significant relation between ROP development and patent ductusarteriosus, intra-ventricular haemorrhage, and hypotension. Chaudhari*et al.*[23] observed insignificant effect of phototherapy on ROP. In multivariate analysis after logistic regression analysis, it was confirmed that low gestational age, sepsis, oxygen therapy, frequency of blood transfusions, history of twins were significant risk factors for development of ROP.The limitation of this study is the small number of patients.

5. Conclusion

The data of this study suggest that low gestational age, sepsis, oxygen therapy, frequency of blood transfusions, twin delivery are independent risk factors in the development of ROP. Clinician should be aware of the presence of additional risk factors when monitoring preterm infants. The timely retinal screening of high risk preterm infants is important to prevent the development of advanced ROP. Since ROP may produce serious sequelae up to complete blindness, all efforts must be made to prevent the development of advanced ROP through reduction of preterm births, changes in the neonatal care, and improvement in detection of threatening ROP markers.

Table 1: Relationship between Retinopathy of Prematurity with demographic profile and various risk factors

S. No	Variables	Number	Case with ROP	Case without ROP	p-value
1	Sex	Male (n 90)	20	70	>0.05
		Female	15	50	

2	Mode of delivery	Vaginal delivery (n 100)	25	75	>0.05
		Caesarean section	10	45	
3	Gestational age	<32 weeks (n 115)	32	93	0.036
		>32 weeks (n 35)	3	27	
4	Birth weight (grams)	<1000g (n 5)	4	1	0.0001
		1000-1500g (n 40)	23	17	
		>1500-2500g (n 70)	6	64	
		>2500g (n 40)	2	38	
5	RDS	n 45	10	35	>0.05
6	Sepsis	n 75	25	50	0.003
7	IVH	n 15	10	5	0.0001
8	Duration of oxygen therapy	<1 week n 5	5	45	>0.05
		>1 week n 75	25	50	
9	Mechanical ventilation	n 10	5	5	>0.05
10	Oxygen therapy	n 65	20	45	0.0126
11	BT given	n 40	38	2	<0.0001
12	CRP positive	n 50	15	35	0.32
13	H/O Twins	n 20	20	0	<0.0001
15	Any significant maternal history	n 45	15	30	>0.05
16	HIE	n 30	5	25	>0.05
17	Phototherapy	n 75	20	55	>0.05

Table 2: Relationship between GA and Stages of Retinopathy of Prematurity (First Detection)

Stages of ROP	<32 weeks with ROP	>32 weeks with ROP	P value
Stage 1 ROP (n= 20)	16	4	0.9
Stage 2 ROP (n=10)	9	1	
Stage 3 ROP (n= 5)	4	1	

There was no significant relationship between gestational age and stages of ROP (p=0.9)

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