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A prospective study to determine the incidence of retinopathy of prematurity at a tertiary care centre in Western Rajasthan and delineate its risk factors

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ABSTRACT

Background: Retinopathy of Prematurity (ROP) is one of the most common causes of preventable blindness in children. Recent advances in the neonatology have increased preterm survival and so has the ROP incidence. Studies all over the world and across the country have shown a wide range for incidence of ROP and so it is difficult to gauge the exact incidence, especially in our region.

Methods: This prospective observational study was conducted in neonatal units of the Department of Paediatrics, Dr. S. N. Medical College, Jodhpur for a duration of six months. All newborns delivered in hospitals associated with Dr S. N. Medical College with gestation age at birth <34weeks and 34-36weeks associated with risk factors subjected to ROP screening by indirect ophthalmoscope by a trained ophthalmologist. Neonates with congenital cataract, hazy cornea, abnormal anterior chamber and those who expired or lost to follow up before sufficient examination could be done were excluded.

Results: Out of 250 newborns screened, 34 (13.6%) were found positive for ROP and out of these 34, 18 (52.94%) had stage I, 11 (32.35%) had stage II, 5 (14.7%) had stage III and none for stage IV and V. Prolonged oxygen therapy, low birth weight, apnoea and sepsis were found to be significant risk factor (p<0.05) with the relative risk of 12.49, 3.71, 3.03 and 1.91 respectively.

Conclusions: ROP is a preventable cause of blindness in children. Thus, its screening is indispensable and it has to be intensified in presence of risk factors such as prolonged oxygen therapy, low birth weight, apnoea and sepsis.

Keywords: Blindness, Incidence, Pre-terms, Retinopathy of prematurity, Risk factor

INTRODUCTION

Retinopathy of Prematurity (ROP) is an important preventable cause of partial or complete loss of vision in prematurely born infants. In the Royal Blind School of Edinburgh, it accounts for up to 10% of childhood blindness. It is characterized by abnormal neovascular developments which are fragile and can leak or bleed,

scarring the retina and pulling it out of position causing a fractional retinal detachment leading to visual impairment and blindness.² Worldwide assessment in 2010 estimated that 21.8% of preterm infants born develop some degree of ROP subsequently.³ In our country, the incidence of ROP is reported to approximately range from 20 to 52% in preterm infants.⁴⁻⁸ Changes in neonatal care have increased the survival of preterm infants and decreased the gestational age at which preterm born infants are kept

alive, resulting in an increasing number of infants at risk for ROP. Previous studies have stated certain risk factors like prolonged oxygen therapy, anaemia needing blood transfusion, sepsis, apnoea and few others which increase the probability of developing ROP.⁴⁻⁸

Visual impairment can be decreased by timely screening, thorough follow up and prompt treatment of neonates who are diagnosed with ROP and offer better overall development for the child. So, a dedicated screening program is indispensable. However, as reported, incidence of ROP strongly depends on the study cohort and the level of care, so screening guidelines cannot be applied uniformly in different countries. For that reason, it is important to define and to inventorize the population at risk for potentially blinding ROP and to provide evidence for a quality guideline in the country, thus we conducted a study to determine the incidence of ROP in Western Rajasthan and its association with risk factor.

METHODS

This prospective observational study was conducted in Division of Neonatology, Department of Paediatrics, Dr. S. N. Medical College, Jodhpur over a period of six months after the approval from Institutional ethics committee on 250 pre-terms.

All neonates with gestational age <34wks at birth and neonates with gestational age 34 to 36wks at birth associated with mechanical ventilation, prolonged oxygen therapy, apnoea, anaemia or blood transfusion were included in the study (using expanded new Ballard score). All neonates who died or lost to follow up before sufficient number of eye examinations could be done to diagnose ROP, neonates with congenital cataract, hazy cornea, abnormal anterior chamber and neonates with consent not given were excluded from the study.

Informed written consent was obtained from the parents and all enrolled newborns were examined after dilating the pupils by the same trained Ophthalmologist with Indirect ophthalmoscopy with a 28D lens with a speculum and scleral depressor to look for the peripheral retina. The ROP was classified by location on the retina (zone 1-3), and severity (stage 1-5), according to the criteria established by the International Committee for Classification of ROP.¹⁰ All patients diagnosed with stage 3 ROP were treated with laser photocoagulation. Birth weight, gestational age at birth, mode of delivery, sex, duration of O₂ therapy and other postnatal events of all the included babies were noted.

The initial eye examinations were done within 28 days after birth (for neonates with gestational age >28wks) and at postmenstrual age of 31 weeks (for neonates with gestational age <28wks). Follow-up examinations was done in a week or 2 on the basis of retinal findings up to full retinal vascularization, regression of ROP or reached threshold for laser treatment.

Keeping the prevalence of 21% (as reported in Gupta VP et al), 95% confidence interval and 0.05 precision errors, the sample size was calculated to be 255. The data obtained was analysed using Microsoft Excel 2010 with the help of SPSS (version 20.0). Continuous data was summarized as mean \pm standard deviation and categorical data as proportion and were analyzed using Fisher exact test and a probability (P) of less than 0.05 was considered significant. Relative risk of each factor was also calculated to find out the most common risk factors in our study.

RESULTS

During this period, total live births (fulfilling inclusion criteria) were 332. Out of them 45 pre-terms expired and 37 were lost to follow up. After excluding them, the study cohort comprised of 250 neonates.

Out of the 250 pre-terms babies screened for retinopathy of prematurity, 34 were found to be positive, thus, the incidence of retinopathy of prematurity in the current study was 13.6% (34/250) and out of these 34 ROP cases, maximum i.e. 18 were in stage I, followed by 11 in stage II and 5 in stage III and nil for stage IV and V. Isolated right eye involvement was seen in 12 pre-terms, isolated left eye involvement in 7 and both eyes in 15.

In our study, out of 137 males (54.8%), 19 showed ROP and out of 113 females (45.2%), 15 were positive for ROP with p=1; 25 out of 205 normal vaginal delivered (82%) had ROP and 9 out of 45 lower segment caesarean section (18%) developed ROP with p=0.22 and 4 out of 28 twins (11.20%), 1 out of 6 triplets (2.4%) and 29 out of 216 single (86.4%) developed ROP with p = 0.9. All were having no significant association with ROP.

Table: 1: Relationship between gestational age and the severity of ROP.

	Gestation age at birth <32 wks (95)	Gestation age at birth ≥32 wks (155)
STAGE I (18)	14 (41.17%)	4 (11.76%)
STAGE II (11)	8 (23.52%)	3 (8.82%)
STAGE III (5)	3 (8.82%)	2 (5.88%)

The mean birth weight of cohort in our study was 1.34 kg \pm 0.21 ranging from 0.95kg to 1.92kg while the mean birth weight of the ROP pre-terms was 1.18 wks \pm 1.24 and the mean gestational age at birth of cohort was 32.83 wks \pm 1.65 ranging from 28wks to 36wks in the study while the mean gestational age at birth of the ROP pre-terms was 30.27 wks \pm 1.54. 95 pre-terms were <32 weeks out of which 25 developed ROP and 155 were \geq 32 weeks out of which 9 developed ROP with p=0.0001 thus, lower gestational age is a significant risk factor with RR of 4.53

(2.21-9.29) but there was no significant relationship between gestational age and the severity of ROP as shown in the Table 1.

In the study, prolonged O₂ therapy, apnoea, low birth weight and sepsis showed a significant association with

ROP (p <0.05) with the relative risk of 12.49, 3.71, 3.03 and 1.91 respectively as shown in the Table 2.

Hypoglycemia, IVH, blood transfusion, PDA, INN and RDS did not show a significant association with ROP (p >0.05) as shown in the Table 3.

Table 2: Association of ROP with various risk factors.

Risk factors	ROP (+) n=34	ROP (-) n=216	P value	RR (95%CI)
Prolonged O ₂ therapy (>1wk)	28	40	0.001	12.49 (4.56-81.42)
Apnea (1 or more episode)	17	36	0.001	3.71 (2.04-6.77)
Low birth wt (<1.25kg)	20	60	0.006	3.03 (1.61-5.69)
Sepsis (Blood culture +)	15	58	0.04	1.91 (1.03-3.55)

Table 3: Relationship with IVH, IVH, blood transfusion, PDA, INN and RDS.

Risk factors	ROP (+) N=34	ROP (-) N=216	P value	RR (95%CI)
IVH (as identified by USG)	3	9	0.21	1.91 (0.68-5.39)
Hypoglycemia (bsl<40)	6	20	0.13	1.84 (0.84-4.03)
Blood transfusion	10	40	0.16	1.66 (0.85-3.25)
PDA (as identified by 2D Echo)	9	42	0.35	1.44 (0.71-2.88)
INN (requiring phototherapy)	17	146	0.06	0.53 (0.28-0.99)
RDS (Downey's > 6)	12	115	0.07	0.52 (0.27-1.02)

DISCUSSION

The present study area belongs to a desert state located in Western Rajasthan, India. Here the incidence of ROP was found to be 13.6% (34/250). This was less than that reported in many other studies such as 28.57% by Parekh A et al (n=154), 53.4% by Gupta N et al (n=350), 21.6% by Rao KA et al (n=282) and 20% by Maheshwari R et al (n=66) in other parts of our country, 29.2% by Shah VA et al (n=564) in Singapore, 19.2% by Hakeem AH et al (n=172) in Egypt and 32.4% by Taqui AM et al (n=68) in Pakistan. 11-16.8 Significantly lower incidence may explained by the fact that these studies involved extremely premature infants also and very low birth weight infants and loss of such infants due to death or lost to follow-up in our study.

However, it is higher than the study done by Chen Y et al (n=639) in Beijing which reported a prevalence of 10.8% as it involved infants with higher gestational age (GA) at birth and birth weight (BW) (up to 2 kg BW and /or 34 weeks GA) and 12.76% by Samatha P et al (n=94) in Mangalore which had pre-terms with GA up to 36 wks or BW up to 2 kg. 17.18

Association with risk factor

Like most other studies, there was no significant association between the gender, mode of delivery and multiple pregnancy with the development of ROP, except in a study done by Agarwal R et al which showed a

characteristically male preponderance and more LSCS delivered preterms showed a significant association with ROP in a study by Shah VA et al.^{19,14} The cause for the same could not be found out.

A significant association with low GA at birth was seen, however, we found no significant relationship between gestational age and the severity of ROP. Similar results were found in a study done by Parekh A et al on 154 preterms where the mean gestational age of ROP babies was 30.1 (\pm 2.0) weeks (p <0.001), significantly less than non ROP babies which was 32.4 (± 1.9) weeks and out of total 44 ROP babies, 36.44% (n=39) of ≤ 32 weeks and 10.63% (n=5) of >32 weeks were ROP (p <0.001) suggesting it to have significant association. Also, in a study on 172 pre-terms at Egypt, 33 had ROP, out of which 45.83% (n=11) of <32 wks and only 14.86% (n=22) of \geq 32 wks pre-terms developed ROP with a p < 0.001 suggesting it to be a significant factor. 11,15 This can be explained by immaturity of vascularization that induces an increased susceptibility of the retina to oxidative damage.

In our study, prolonged O_2 therapy showed a significant association. Similarly, in the study done at Egypt, 22 (26.5%) out of 83 pre-terms with O_2 therapy developed ROP while only 11 (12.35%) out of the other 89 pre-terms who were not exposed to O_2 developed ROP suggesting it to have a significant association (p=0.018) with the relative risk (RR) of 2.14 (1.10-4.14) and in the study done at Bangalore, O_2 therapy for >3days and ROP

had a significant association (p=0.01) with the relative risk (RR) of 1.57 (1.15-2.13). Similar significant association with O_2 therapy was also seen in the studies by Gupta VP et al (p=0.01) and Chaudhari S. et al (p=0.03). However, no significant association with O_2 therapy was seen in the study done by Samatha P et al (p=0.09).

Like in our study, in a study done at Pune, 19 (52.77%) out of the 36 apnoeic pre-terms developed ROP while other 25 pre-terms (21.18%) were out of the 118 who did not have apnoea suggesting it to have a significant association with ROP (p=0.001) with the RR of 3.08 (1.57-6.94). Similar significant association with apnoea was also seen in the studies by Gupta VP et al (p=0.02), Chaudhari S. et al (p=0.001), Aggarwal R et al (p=0.001) and Chen Y et al. 4.19.17 But, no significant association with apnoea was seen in the study done by Swarna R et al and Gupta N et al. 12

We found low birth wt to have a significant association with ROP, similarly, in a study done by Parekh A et al, 27 (55.1%) out of the 49 low birth weight pre-terms developed ROP and only 17 (16.19%) out of the other 105 pre-terms had ROP suggesting low birth weight to be a significant factor for ROP (p=0.001) and the relative risk (RR) was found to be 4.88 (2.01-9.59). Similar significant association with low birth weight was also seen in the studies by Gupta VP et al (p=0.02), Rao KA et al (p=0.01), Shah VA et al and Chen Y et al. 5,13,14,17 However, no significant association with low birth weight was seen in the study done by Swarna R et al (p=0.09) and Hakeem AH et al (p=0.10). 6,15

Sepsis was found to be significant factor for ROP like in a study at Egypt, 29 (25.21%) out of the 115 septic preterms were found to have ROP while only 4 (7.01%) out of the other 57 pre-terms developed ROP suggesting sepsis to have a significant association with ROP (p=0.004) with the RR of 3.59 (1.32-9.72). Similar significant association with sepsis was also seen in the studies by Gupta VP et al¹² (p=0.04), Aggarwal R et al¹⁹ (p=0.001) and Chaudhari S. et al (p=0.001). However, no significant association with sepsis was seen in the study done at Pune (p=0.34) and Mangalore (p=0.48). In this may be explained by the effect of endotoxins due to sepsis on retinal blood vessels.

CONCLUSION

There were certain limitations like there were very less pre-terms born less than 30 weeks and all those born did not survive or follow up till ROP screening was completed, which is the cause of low incidence in our study. Antenatal factors including PIH, GDM, maternal anemia, antenatal steroids and postnatal factors like hypocalcaemia, thrombocytopenia, polycythaemia and postnatal weight gain were not evaluated as in other studies. Few ROP cases in late pre-terms with GA at birth >34wks were missed.

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