

Original Research Article

Prevalence and outcome of retinopathy of prematurity in preterm infants, with low birth weight at KMCH, Tamil Nadu, India

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ABSTRACT

Background: Premature infants have avascular or incompletely vascularized retina at birth and ROP evolves over 4-5 weeks after birth. The aim of this study is to know the prevalence of retinopathy of prematurity in preterm infants, with birth weight ≤ 1500 grams and/or gestational age ≤ 32 weeks in a tertiary care center.

Methods: The study was conducted in Kovai Medical Centre and Hospital Coimbatore in 2016. The sample size is 95 babies. All preterm infants admitted with a birth weight of ≤ 1500 grams and/or ≤ 32 weeks of gestation and baby those at risk of ROP.

Results: 95 babies have enrolled during the study period of which 78 babies fulfilled the inclusion criteria and completed this prospective study. 12 babies could not complete the follow-up protocol and 5 babies died before full vascularization of the retina. 78 babies who fulfilled the inclusion criteria were screened and 15 babies were found to have ROP. The prevalence of ROP in this study is 19.2%.

Conclusions: Among the preventable causes of blindness in children, ROP figures very high on the agenda. Low birth weight and gestational age were found to be the most important risk factors for the development of ROP.

Keywords: Low birth weight, Oxygen therapy, Prematurity in preterm infant, Retinopathy

INTRODUCTION

In 2010, an estimated 39 million people were blind in the world, of which childhood blindness accounted for 4%. Among avoidable and treatable causes, retinopathy of prematurity (ROP) is an emerging etiology.¹ Globally, there are at least 50,000 children blind from ROP, which remains an important cause of childhood blindness in high-income countries and is also emerging as a major cause of childhood blindness in middle-income economies, such as Latin America, Eastern Europe, India, and China.² Retinopathy of Prematurity (ROP) is a vasoproliferative 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.

Premature infants have avascular or incompletely vascularized retina at birth and ROP evolves over 4-5 weeks after birth.³ This relatively slow evolution gives a small window of opportunity to effectively conduct retinal examinations and timely interventions to improve visual outcome and avoid irreversible blindness due to retinal detachment from progressive untreated ROP.⁴ The incidence of ROP in India is reported to vary between 38-51.9 % in low birth weight infants. ROP in high-income countries now occurs, mostly in extremely low birth weight infants.⁵ In those countries, the incidence of ROP seems to have declined incrementally over the last few decades. But in middle-income countries like India, high rates of premature birth and increasing resuscitation of premature infants, often with suboptimal standards of

care have resulted in an epidemic of ROP.⁶ Improved maternal and neonatal care, ROP screening guidelines appropriate to middle-income countries, and widespread timely treatment is urgently called for to control this epidemic.⁷

METHODS

The study was conducted in Kovai Medical Centre and Hospital Coimbatore. The sample size is 95 babies. All preterm infants admitted with a birth weight of ≤ 1500 grams and/or ≤ 32 weeks of gestation and baby those at risk of ROP.

Inclusion criteria

- Premature infants admitted with ≤ 32 weeks gestation and/or birth weight ≤ 1500 g.
- Babies between 1501-2000 g and/or 33-35 weeks who are at a higher risk of developing ROP like, respiratory distress syndrome, sepsis, multiple blood transfusions, multiple births, apneic episodes, intraventricular hemorrhage.

Exclusion criteria

- Babies from whom consent for the study could not be obtained.
- Babies who died before full vascularization of the retina.

First examination

A first screening examination was carried out at 32 weeks of gestation or 4 weeks of age, whichever was later. For this purpose, gestational age was calculated from the last menstrual period or with the help of the first-trimester sonography in cases where the last menstrual period date was uncertain. Sometimes the babies were examined earlier in the case of extremely premature neonates.

Procedure

All preterm babies who satisfied any one of the inclusion criteria were taken up for the study. Demographic history and risk factors like respiratory distress syndrome, sepsis, multiple blood transfusions, multiple births, apneic episodes, and oxygen are given were documented using a study Proforma.

Preparation of the child

The pupils were dilated with a mixture of Phenylephrine 2.5% and Tropicamide 0.5% instilled 3 times at 10 minutes interval about 1 hour before the scheduled examination. Resistance to dilation was noted. Care was taken to wipe off any eye drops with sterile cotton that comes out of eyes to cheeks and not to feed the baby immediately before examination as the child might vomit or aspirate.

Method of examination

The examination was done under aseptic precautions in a temperature-controlled room by an ophthalmologist in the presence of a neonatologist. The indirect ophthalmoscopic examination was done. One drop of topical paracrine eye drops was used to anesthetize the cornea. A pediatric wire speculum was used to keep the eyelids apart. After decreasing the room illumination, the anterior segment was first visualized to look for tunica vasculosa lentils, pupillary dilatation and lens, and media clarity. Then the posterior pole was examined for any Plus disease. A scleral indenter was used to visualize the periphery. The periphery was examined in all clock hours to look for the extent of changes from nasal to the temporal retina. Care was taken not to put too much pressure on the globe. During the examination, untoward neonatal complications were looked for and managed appropriately.

Follow up protocol

If no ROP was detected at initial examination, the infants were re-evaluated once every two weeks until vascularization was complete. If ROP was detected, the examinations were performed weekly for stage 1-2 disease and more frequently for stage 3 disease, till the disease started resolving or progressed to threshold stage. Babies showing evidence of regression were followed up till vascularization was complete. Babies progressing to threshold stage were advised treatment. The follow-up examinations were done at the Neonatal Intensive Care Unit itself if the baby had to stay there for some other reasons. The discharged babies were called up for follow up as advised by the ophthalmologist.

Statistical analysis

Data were analyzed using SPSS software version 22 and MedCalc software version 15. Data were interpreted using descriptive and inferential statistics. The student 't' test was used to determine whether there was a statistical difference in weight, gestational age, postconceptional age at first examination between babies who had ROP and those babies who did not have ROP. In the entire test, the "p" value of less than 0.05 was accepted as indicating statistical significance. Data analysis was carried out using the Statistical Package for Social Science (SPSS-20) package.

RESULTS

95 babies were enrolled during the study period of which 78 babies fulfilled the inclusion criteria and completed this prospective study. 12 babies could not complete the follow-up protocol and 5 babies died before full vascularization of the retina. Out of 78 babies screened, 44 were male and 34 were female. The birth weight of the study population ranged from 550 g to 2000 g with a mean birth weight of 1190 ± 297.03 g.

Table 1: Prevalence of retinopathy of prematurity (any stage).

ROP	No.	%
Present	15	19.23
Absent	63	80.77
Total	78	100

78 babies who fulfilled the inclusion criteria were screened and 15 babies were found to have ROP. The prevalence of ROP in this study is 19.2%. Out of 15 babies with ROP, 6 babies (40%) were in stage 1, 6 babies (40%) were in stage 2 and 3 babies (20%) were in stage 3 (Table1).

Table 2: Type of gestation.

Type of gestation and ROP				
		ROP		Total
		Present	Absent	
Type of gestation	Single	8	36	44
	Twin	7	27	34
	Total	15	63	78

Out of 78 babies, 44 babies were singletons, 34 babies were twins. Out of 44 singletons, 8 babies developed ROP. Only 7 of the 34 twins developed ROP. Type of gestation was not found to be significantly associated (p=0.789) with ROP in the present study (Table 2).

Table 3: Birth weight and ROP.

Distribution as per birth weight				
		ROP		Total
		Present	Absent	
Birth weight	≤1000g	12 (48%)	13 (52%)	25
	1001-1500g	3 (6.98%)	40 (93.02%)	43
	>1500g	0	10 (100%)	10
	Total	15	63	78

The birth weight of the ROP babies ranged from 550-1460 g (mean 884.33±221.75g), while that of non-ROP babies ranged from 780-2000 g (mean 1270.25±263.38g). Lower birth weight was significantly associated with increased incidence (p <0.001) of ROP. The incidence of ROP was 48.0% in Extremely low birth weight babies weighing ≤1000g at birth, while in the very low birth weight group weighing 1001-1500g at birth was 6.97%. The only baby with Severe ROP had a birth weight of 660g (Table 3).

The gestational age of the ROP babies ranged from 26-32 weeks (mean 27.60±1.72 weeks), while that of non-ROP babies ranged from 27-34 weeks (mean 30.59±1.71 weeks). The incidence of ROP was 83.3% in babies born <28 weeks of gestational age. Among babies born between 28-32 weeks of gestation, the incidence of ROP was 8.3%. Lower gestational age was found to be a

significant risk factor for the development of ROP (p <0.001). The only baby who had severe ROP was delivered at 27 weeks of gestation (Table4).

Table 4: Gestational age and ROP.

Distribution of gestational age				
		ROP		Total
		Present	Absent	
Gestational age	<28	10 (83.3%)	2 (16.7%)	12
	28-32	5 (8.3%)	55 (91.7%)	60
	>32	0 (0%)	6 (100%)	6
	Total	15	63	78

Out of 78 babies screened 51 were given oxygen and 15 (29.41%) babies developed ROP. None of the babies for whom oxygen was not given developed ROP. Oxygen administration was a significant risk factor for the development of ROP (p <0.001) (Table 5).

Table 5: Oxygen and ROP.

Oxygen and ROP				
		ROP		Total
		Present	Absent	
Oxygen	Given	15 (29.41%)	36 (70.59%)	51
	Not given	0	27 (100.0%)	27
	Total	15	63	78

DISCUSSION

Retinopathy of prematurity (ROP) is a vaso-proliferative disorder affecting premature infants. It is one of the most common causes of visual loss in children and can lead to lifelong vision impairment and blindness.⁸ Low birth weight and gestational age were found to be the most important risk factors for the development of ROP. With neonatal units equipped with the state-of-the-art technological background and highly qualified personnel providing optimum care of extremely premature newborns, ROP incidence is on a rise due to improved survival rates of premature neonates in many neonatal units.⁹ Authors screened babies admitted to present neonatal intensive care unit with birth weight ≤1500g and gestation ≤32 weeks. Infants with birth weight >1500g and gestation more than 32 weeks were screened only if they had additional risk factors.¹⁰ All India Institute of Medical Sciences, New Delhi in their recent protocol have suggested similar screening criteria. In India, large, relatively mature babies with BWs more than 1500g and Gas more than 34 weeks or so have been reported to have high incidences of severe ROP since the early 1990s.¹¹ In a retrospective study of 138 patients with BWS more than 1250g referred for ROP examination, Darlow BA reported that 45% had a threshold or worse ROP, demonstrating that severe ROP occurs in bigger babies in India. present study included 78 neonates who were screened for ROP and 15 babies among them were found to have ROP.¹² The prevalence of severe ROP in the

study is 1.28%. It is of current knowledge that, aggressive posterior ROP seems to occur especially among smaller and more immature neonates. However, in present study, authors did not have babies who developed APROP. None of the babies in present study had blindness due to ROP. The incidence of ROP from studies done in the Indian subcontinent was found to be 17.5%-46% whereas the incidence of ROP in different studies done outside India was found to be 9.4%-38%.¹³ Among the Indian studies, Fortes Filho et al reported overall incidence as 17.5 % and no severe ROP. It was comparable to present study. They had studied 40 babies with <32-week gestational age, but the birth weight criteria in their study were <1250g. The incidence of a severe form of the disease (threshold disease) is decreasing.¹⁴ The occurrence of Severe ROP is very less in present study compared to other studies from India Gilbert C et al and co-workers also found a drop from 46 to 21% in their study over a period of 7 years. While the prevalence of ROP (of any stage) was comparable, the prevalence of severe ROP was low in present study compared to other Indian studies.¹⁵ The prevalence of ROP was 48.0% in extremely low birth weight babies weighing ≤ 1000 g at birth, while in the very low birth weight group weighing 1001-1500 g at birth was 6.98%. None of the babies >1500 g had ROP.¹⁶ Low birth weight was identified as a risk factor for ROP in several International and Indian studies. The CRYO-ROP multicenter study (1986-1987) showed that among infants with BW <1251g, 65.8% developed ROP to some degree, and the incidence was 81.6% in infants <1000 g. In a study by Gopal L et al, overall incidence among infants with BW <1001g was 46%, which was almost similar to present study.¹⁷ Moreover, none of the infants in both studies with BWs >1000g reached the threshold for laser or cryotherapy. In India, large, relatively mature babies with BWs more than 1500 g and GAs more than 34 weeks or so have been reported to have high incidences of severe ROP since the early 1990s.¹⁸ For example, Gunn DJ, reported in 2012 an overall incidence of 47% ROP in their babies with BWs of 1700 g or less, with an incidence of 12.8% requiring treatment; this figure has changed little over the 15 years or so. In a retrospective study of 138 patients with BWs, more than 1250g referred for ROP examination. Lower Gestational age was found to be a significant risk factor for the development of ROP ($p < 0.001$) in this study.¹⁹ The gestational age of the ROP babies ranged from 26-32 weeks (mean 27.60 ± 1.72 weeks), while that of non-ROP babies ranged from 27-34 weeks (mean 30.59 ± 1.71 weeks). The prevalence of ROP was 83.3% in babies born < 28 weeks of gestational age. Among babies born between 28-32 weeks of gestation, the prevalence of ROP was 8.3%. None of the babies delivered >32 weeks of gestation had ROP.²⁰ Out of 78 babies screened 51 were given Oxygen and 15 (30.00%) babies developed ROP. The causal link between ROP and supplemental oxygen has been confirmed by controlled trials and clinical studies.²¹ Kong L analyzed data from their low birth weight survivors and found a significant association between, the more severe grade of cicatricial disease and

duration of oxygen therapy. Oxygen as a risk factor for ROP in different studies in India has been established.²² In a recent study it has been found that exposure to unblended oxygen causes massive retinovascular vessel loss and that causes aggressive posterior ROP in large preterm babies. NEOPROM collaborative study which is a meta-analysis of 5 larger trials comprising 4,911 infants, concluded that in babies <28 weeks' gestational age low saturation targets (85-89%) until 36 weeks postmenstrual age are associated with more deaths and more NEC and higher saturation targets (91-95%) are associated with more ROP.²³⁻²⁵

CONCLUSION

ROP screening programme should include neonates with birth weight <1500g and/or gestational age <32 weeks and babies more than 1500g and >32weeks with other risk factors of ROP. Along with the regular screening, each neonatal unit should have a policy on oxygen administration. Pulse oximeters and blended oxygen should be used in delivery rooms and neonatal units to guide oxygen therapy. All babies who receive oxygen should be monitored closely to target oxygen saturation of 90-95% with appropriate use of oxygen blenders.

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