INCIDENCE AND RISK FACTORS OF ROP IN A TERTIARY CARE CENTER IN WESTERN ODISHA: OUR EXPERIENCE SO FAR

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ABSTRACT

BACKGROUND

Retinopathy of prematurity (ROP) is a disorder of preterm infants in which the developing retinal blood vessels are not well developed which causes poor visual acuity or blindness. Blindness due to retinopathy of prematurity (ROP) or severe visual impairment can be prevented if at risk infants are screened before occurrence of advanced stages of ROP. This study was done to determine the incidence of ROP in western Odisha so far and the risk factors associated with it.

METHODS

Demographic factors and clinical information of all the 160 consecutive infants screened for ROP in Dept. of Ophthalmology, VIMSAR, Burla were recorded and thoroughly analysed. Infants' gestational age (GA), PMA (postmenstrual age), birth weight (BW), gender, singleton or multiple births, being the first child, and their NICU/neonatologist's recommendation for eye examination were recorded based on their medical records. Mothers' LMP, delivery method, EDD were also inquired. Exposure to oxygen supplementation, history of neonatal sepsis, RDS, neonatal jaundice, blood transfusion, convulsion were also recorded according to medical records and databases are accordingly analysed univariately.

RESULTS

Among 160 eligible infants, 125 (78.1%) were found to have associated risk factors other than prematurity (group B), while 26.8% were only premature babies without any other risk factors (group A). Mean age at first eye exam in group A was 35 weeks of PMA versus 32 weeks in group B. The incidence of stage 4 and/or 5 was nil. Being the first child and single or multiple births did not contribute to the time of first eye exam significantly and neither did gender of the infant.

CONCLUSIONS

Providing sufficient information about ROP to parents and educating them about this potentially blinding condition is a must, so that blindness due to ROP can be checked by increasing the chance of on-time screening.

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BACKGROUND

It is estimated that the number of children with low vision would be 3-4 times more, with a number of about 5 million children worldwide. Controlling childhood blindness is one of the priorities of the World Health Organization's (WHO's) Vision 2020-The right to sight program. It is a serious complication in eyes of preterm neonates and remains a major cause of childhood blindness worldwide, although there has been huge advances in the neonatal care system in our country.[1] Both oxygen toxicity and hypoxia contributes to the development of ROP and it was first reported by Theodore L. Terry in 1942.[2]

According to the program different targets have been looked upon, one of them is to control blindness due to retinopathy of prematurity (ROP). Although there are current treatments for ROP which can treat many infants from progressing to its severe forms and blindness, but still evidences are found that some infants still suffer from severe visual disabilities as a consequence of this disease.

ROP is a multifactorial disease involving several factors like Low-gestational age, low-birth weight, sepsis, oxygen therapy, respiratory distress syndrome, and blood

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transfusion.[3] as evidenced by other studies the most significant risk factors for development of ROP were low-gestational age and low-birth weight.[4] Low-gestational age and ROP were found to have the maximum relationship to each other, which is evidenced by the results of studies done by Shah et al.,[5] Karna et al.,[6] and Fortes et al.[7]

In our study, we tried to find out incidence and various risk factors associated with development of ROP in infants in our region who were subjected to examination for ROP screening in our tertiary health care hospital in western Odisha.

METHODS

Settings

This is a cohort study conducted in Dept. of Ophthalmology of VIMSAR, Burla, Odisha during July 2017 to July 2018, with prior consent from the ethical committee of VIMSAR. The parents of infants included in the study were explained about the examination procedure and consent for fundus examination with indirect ophthalmoscopy after dilating the pupils of all infants in group was taken. Most of the infants were screened for ROP in our department, those who were discharged from NICU before 4 weeks, were recommended to seek care after their discharge and those with prolonged NICU admission are transferred by the NICU physicians/ staff to eye hospitals to perform screening examinations. However, nowadays the number of infants who are screened in NICU are increasing but follow up of those patients are quite a difficult task because of lack of awareness among the parents.

In our study, the details of all premature infants who had been screened for ROP were recorded and infants who did not have any recommendation by NICU staff or neonatologist and those who already had passed the golden time of screening were excluded. The study included all premature babies born before 34 weeks and <1500gm. Our study also analysed and documented details of 160 infants screened for ROP.

Data Gathering and Examination

Infants' gestational age (GA), birthweight (BW), gender, singleton or multiplebirths, being the first child, and their NICU/neonatologist's recommendation for eye examination were recorded based on their medical records. Mothers' LMP, delivery method, EDD were also inquired. Oxygen supplementation, history of neonatal sepsis, RDS, NICU stay, neonatal jaundice, blood transfusion, convulsion were also recorded according to medical records. Their age at first eye examination were recorded and indirect ophthalmoscopy using +20 D lens was done after full dilation of both pupils by tropicamide 0.5% and phenylephrine 2.5%. The staging and Grading of ROP was done according to the international classification of ROP.

Parents who brought their infant(s) too late were interviewed to find their delay reason using open questions.

Definitions

The International Classification of Retinopathy of prematurity has described ROP by location (zones) and severity (stages) and defines plus and pre-plus disease. The important definitions are summarized in Table below.

Classification of Retinopathy of Prematurity

Stage 0 - Immature Retina.
Stage 1 - Demarcation line separates avascular from vascularized retina.
Stage 2 - Ridge arising in region of demarcation line.
Stage 3 - Extraretinal fibrovascular proliferation/ neovascularization.
Stage 4 - Partial retinal detachment.
A- Macula Spared
B- Macula Involved
Stage 5 - Total retinal detachment Pre-plus disease More vascular tortuosity than normal, but insufficient for diagnosis of plus disease Plus disease Vascular dilation and tortuosity of at least two quadrants of the eye.

When Should Initial Screening be Performed-

- Infants with GA <30 weeks - initial screen at 3 weeks after birth.
- Infants with GA of <34 weeks - initial screen at four weeks' CA.

Which Infants Should be Screened

GA -<34 wks., BW -<1500 gm

Current Evidence Suggests that Screening Infants with the Following

• GA of 30 6/7 weeks or less (regardless of birth weight); and

• Birth weights of 1250 g or less as recommended by the United Kingdom, is an appropriate strategy with a very small likelihood that an unscreened baby would have treatable ROP. Individual centres may choose to extend birth weight screening criteria to 1500 g, as recommended by the AAP. Screening of infants with birth weights of between 1251 g and 2000 g is appropriate if the neonatologist believes the baby to be at high risk because of the severity and complexity of the neonatal clinical course. Risk factors may include severe and unstable respiratory disease, hypotension requiring inotropes and prolonged ventilator or oxygen therapy. Who should conduct screening Ophthalmologists skilled in the identification of ROP including location and staging as described in the International Classification of Retinopathy of Prematurity revisited.

Follow-Up Examinations

Follow-up examinations should be recommended by the examining ophthalmologist. The AAP suggested schedule is the following:

One week or less follow-up:

- Stage 1 or 2 ROP in zone I
- Stage 3 ROP in zone II.

One- to two-week follow-up:
- Immature vascularization (stage 0) in zone I
- Stage 2 ROP in zone II
- Regressing ROP in zone I.

Two-week follow-up:
- Stage 1 ROP in zone II
- Regressing ROP in zone II.

Two- to three-week follow-up:
- Stage 1 or 2 ROP in zone III
- Regressing ROP in zone III.

Those infants who were premature with low Birth Weight only without any risk factors were grouped under Group A and rest premature infants with risk factors other than Low Birth Weight were included in Group B. Other risk factors include CPAP, RDS, Jaundice, sepsis, IVH, Phototherapy, blood transfusion etc.

RESULTS

During the study period, 240 infants were examined in Dept. of Ophthalmology, VIMSAR, Burla. Among them, 160 infants were found eligible for the study and the rest were excluded. The reasons for exclusion were- not having any recommendation for eye examination by their neonatologist (20%), failed to follow up (55%) and unavailable data about the result of eye exams in the rest. Out of 160 infants screened 102 infants presented during 28 weeks to 42 weeks and 58 Infants presented late, although recommended for ROP screening by NICU staff due to negligence by parents and unawareness of the fact that babies at risk must be screened for ROP before the disease advances and that the risk of advancement of disease increases with increasing age if they have associated risk factors. Many parents were even unaware of the facts that ROP might lead to an irreversible stage which may lead to irreversible blindness of the infants. Among those infants screened 113 infants (70.6%) were male and 47 (29.3%) were females. Out of 113 males, 44.2% of male infants and 65.9% of female infants had ROP. Out of 160 babies examined in our study, 129 (80.6%) were born by singleton pregnancies and 31 babies (19.3%) were born as twin babies. Triplets and quadruplets were not found during our study course. Out of 129 babies born as singleton pregnancy, 70 (54.2%) infants had ROP but out of 31 infants born as multiple pregnancies 11 (35.4%) infants had ROP. Out of the twin babies 2 babies were reproduced by means of in vitro fertilization technique. Maximum babies i.e. 115 (71.9%) were delivered by Normal vaginal delivery and the rest 28.1% were delivered by LSCS. Out of the 115 58 infants had ROP but infants born by LSCS were 45 in total, out of them 23 (51.1%) had ROP which was statistically significant with p- value of 0.04. Out of 140 infants born as 1st pregnancy 71 (50.7%) infants had ROP but only 20 infants as 2nd pregnancy were examined and 10 out of them had ROP.

Mean GA was 34 weeks and mean BW was 1450 gms. It has been found in our study that the BW of babies born as twins was between 900 gm -1200 gm. 125 infants of BW <1500 gm were examined and 57 of them had ROP which was statistically significant with p- value of 0.016. Out of 104 infants with history of RDS 48 infants had ROP with an odds ratio of 1.674(>1). Out of 112 infants with history of sepsis 51 had ROP with both of them statistically non-significant.

10 infants with history of jaundice out of 36 infants had ROP with a p value of 0.02 which was found to be statistically significant and had an odds ratio of 3.483 (>1).only 6 infants out of 15 infants with history of IVH had ROP which was statistically significant and with an odds ratio of >1.21 infants had history of blood transfusion and out of them 12 infants had ROP, with and odds ratio of 0.739 (<1). Out of 37 infants with history of phototherapy 8 infants had ROP and had an odds ratio of 5.293 (>1). The most important risk factor i.e. history of CPAP was found in 106 babies and out of them 51 infants had ROP. But 39 infants who were given oxygen supplementation for more than 7 days and among them 15 infants had ROP with an odds ratio of 1.372(>1). 68 infants had SNCU stay after birth for >15 days, among them 36 infants developed ROP with an odds ratio of 1.365(>1).

On multivariate analysis apart from LBW and low GA statistically significant risk factors associated were RDS (OR 1.674), phototherapy(OR 3.483), IVH (OR >1), blood transfusion (OR 0.739), CPAP (P value 0.04) and O2 supplementation (OR 1.372).

The incidence of ROP was 27.5% (44/160) which is produced in pie chart 1. Out of which 28 were male infants and 16 were female infants. 4 babies among the total had rigid pupils so all zones could not be examined properly in them.

Only 1 infant presented to us between 28-30 weeks of PMA, which was found to have ROP with stage 0, zone I. Among 12 infants who presented within 30-32 weeks of PMA 5 infants were found to have ROP and among them 3 infants has stage 0, zone III retina and the rest 2 has stage 1, zone III and their BW ranged from 950 to 1010 g. 32 infants presented at 32-34 weeks of PMA group and among them 9 infants had ROP, of which 4 infants were found to have stage 0, zone III ROP, 3 infants had stage 1, zone III ROP and 2 among them had stage 3, Zone III, BW of these 9 infants was between 1100 gm- 1320 gm. Maximum number of infants presented to us between 34-36 weeks, i.e. almost 61 infants among which 21 were found with ROP. Out of 21 infants 14 infants had stage 1 zone III, 5 infants had stage 2, zone III and only 2 infants had stage 3, zone III. These infants were found to be within 1400-1650 gm of BW. Subsequent age groups, i.e. 36-38 weeks of PMA had 26 infants who presented to us and among them 8 infants were screened as ROP infants, 5 among them were in stage 1 zone III and 3 infants were in stage 3 zone II; the mean BW in this age group was 1712 gm. 13 infants were screened in the age group of 38- 40 weeks of which only 1 infant was found to have ROP stage 3 zone II with a mean BW was

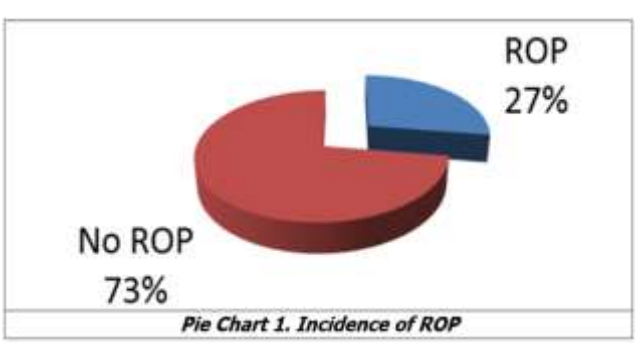
2000 gm. 15 infants were brought to us at or above 40 weeks of PMA and almost all babies had regressing ROP.

Maximum cases were diagnosed as stage 0 zone III and most of them were regressing ROP. 2 APROP cases were diagnosed in zone I with PrePlus disease, thus were referred to higher centers for evaluation and immediate management.

In our study as we divided the infants screened into two groups, Group A included 27(16.8%) infants without any other risk factor other than CPAP while Group B had 133 (83.1%). 39% of group A had their first eye exam before 6 weeks of infantile age while 57% of group B. Mean age at first eye exam in group A was 35 weeks of PMA versus 32 weeks in group B. The incidence of ROP did not have a significant difference in infants examined before and after 9 weeks. None of these infants had stage 4 or stage 5 of ROP. Data on the reason of the delay in group A was available in 8 (36.6%) out of 22 infants presenting late of this group. Among them, 6 incriminated lack of knowledge about the importance of time in ROP, 2 did not know where to seek for screening, 1 had thought that the baby is too small and weak for such examination. In the group B, 9 infants presented late and data of the reason of delay was available in 44.4% (4 infants); among them were seeking medical care in other centers for cardiology abnormalities and developmental hip dysplasia. Univariate analysis showed that infants with first eye exam of above 9 weeks were more likely to be in group B as they had lower GA and lower BW (VLBW, XLBW), admitted immediate post-delivery to NICU for various complications like IVH, neonatal jaundice, RDS, neonatal sepsis, convulsions etc; but gender, being the first child and being born by single or multiple-gestation pregnancies did not contribute to the time of first eye exam. In multiple logistic regression analysis, recommendation type had a significant effect on on-time attendance rate after controlling for GA; we found out that being in group A is associated with 5 times increase in the odds of having eye exam after 9 weeks (Table 2).

	Screened	ROP
Male	113	28
Female	47	16

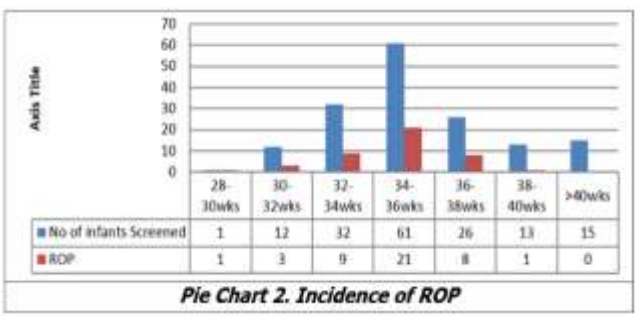
Table 1. Male Female Ratio for Screened and ROP Infants



Pie Chart 1. Incidence of ROP

Risk Factors	No. of Babies Screened with	ROP
Prematurity	160	44 (100%)
VLBW	142	17 (38.6%)
XLBW	18	9 (20.4%)
Respiratory Distress Syndrome	106	23 (21.6%)
Neonatal Sepsis	79	18 (22.7%)
Neonatal Jaundice	79	26 (32.9%)
Gender (male)	113	28 (24.7%)
1st Child	148	12 (27.2%)
Multiple Birth	96	6 (13.6%)
Assisted Delivery	23	6 (26.08%)
Intraventricular Haemorrhage	15	9 (60%)
Convulsions	22	1 (2.2%)
Blood Transfusion	21	9 (42.8%)

Table 2. Risk Factors Associated with ROP



Pie Chart 2. Incidence of ROP

DISCUSSION

ROP is a disorder of retinal vascular development in preterm infants exposed to oxygen supplementation. One of the major causes of development of severe ROP and blindness due to ROP in our region is unawareness among the parents for the need of ophthalmological examination in the infants subjected to these risk factors.

The incidence of ROP in this study was 27.5% compared to incidence reported in many other studies; 24% in India,[8] 29.2% in Singapore,[5] and 32.4% in Pakistan.[9] However, in our study only 9 out of 54 infants with high gestational age had ROP as compared to the study which included babies with higher gestational age and birth weight with a prevalence of 10.8%.[10]

Risk Factors

In our study, on multivariate analysis low-gestational age, sepsis, RDS, jaundice, BW, intraventricular haemorrhage, duration of oxygen therapy >7 days, CPAP for >7 days, SNCU stay >15 days and blood transfusion were found to be risk factors for development of ROP. Meanwhile, sex, mode of delivery, gender, multiple pregnancies were nonsignificant risk factors by using univariate analysis. In our study, we found that sepsis was significantly associated with the development of ROP like in Shah et al.,[5] and Vinekar et al.[11] On the other hand, Chaudhari et al.,[12] and Smith[13] showed an opposite result.

In our study we found that GA and severity of ROP was not statistically significant, but this was in disagreement with other studies[5, 3] showing that lower GA was associated with severe ROP.

Some studies reported that duration of oxygen therapy more than 7 days was a significant risk factor for development of ROP [5,14] and in our study also we found it as significant. Our study showed mechanical ventilation and CPAP are significant risk factors for ROP and this agreed with chaudhury et al.[5,12]

In our study, we found that blood transfusions is a risk factor for development of ROP, and this was similar to Deepak et al.[15] Our study revealed no statistical significant relationship between sex and occurrence of ROP, in contrast to Darlow et al.,[16] which found that male sex is a risk factor of development of ROP. As Seiberth and Lindarkomp elaborated,[17] we too found insignificant relationship between the mode of delivery and occurrence of ROP having any relationship to each other. Rather hirano et al.,[18] stated that it is controversial and iron overload rather than number of transfusions which contributed to the development of ROP.

Taqui et al.,[9] reported no significant relation between ROP and intraventricular hemorrhage but observed a significant relation between RDS and the development of ROP as we did. Chaudhari et al[12] observed an insignificant effect of phototherapy on ROP and so as we. Gupta et al[19] reported relation of RDS to development of ROP.

Low-gestational age was found to be a very significant risk factor of ROP in our study, this was in agreement with Shah et al., [5] Karna et al.,[6] and Fortes et al.[7] But this was in disagreement with other studies,[5,3] showing that lower gestational age was significantly associated with only severe ROP.

We found that birth weight was not a statistically significant factor for the development of ROP which is similar to Arroe and Peitersen.[20] We found that birth weight was an insignificant factor for development of ROP not in agreement with many studies[5,7,21] 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 transfusion in very low birth weight infants and thus development of ROP. This statistic was attributable to the small number of patients (3 out of 172 cases) whose birth weight was <1000g.

In our study, we found that sepsis was significantly associated with the development of ROP like Shah et al.,[5] and Vinekar et al.,[11] but this was in disagreement with the results of Chaudhari et al.,[12] and Smith.[13]

Oxygen therapy was an independent risk factor of ROP.[5,8,22] We found a significant relationship between ROP and use of oxygen therapy, on the other hand, Palmer et al.,[23] reported that oxygen therapy was a nonsignificant factor for ROP. We found that Oxygen therapy >7 days as an association factor for development of ROP as in other studies which reported that a duration of oxygen therapy >7 days was a significant risk factor in development of ROP.[5,14] but Dutta et al contradicted the fact.[24] We found that mechanical ventilation and CPAP were significant risk factors for ROP and this was unlike Murthy et al.[8]

CONCLUSIONS

The prevalence of ROP in this study was 27.5%, which suggests that low gestational age, oxygen therapy, RDS, jaundice, phototherapy, CPAP, longer SNCU stay, IVH and blood transfusion are important risk factors in the development of ROP. The high-risk preterm infants must be subjected to timely retinal checkup to prevent the development of advanced ROP and thus prevent childhood blindness due to ROP. Awareness of the fact that ROP must be ruled out in the presence of the various above-mentioned risk factors which are independently responsible for changes in the neonatal care, must be created.

The limitation of this study is the small number of patients in our region.

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