



INCIDENCE AND RISK FACTORS OF RETINOPATHY OF PREMATURETY: A CLINICAL STUDY CONDUCTED AT TERTIARY CARE HOSPITAL

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ABSTRACT Retinopathy of prematurity is a disease of retinal vasculature seen in preterm babies. Though oxygen administration was considered as one of the major causes for preventable childhood blindness worldwide. A hospital based study was conducted on 100 babies attending ROP screening in Regional Eye Hospital, Kurnool from November 2019 to October 2021. Detailed birth history and history of risk factors were noted and dilated fundus examination was done with indirect ophthalmoscopy with the aid of eye speculum and scleral depressor. Screening and follow-up schedule was done according to ETROP guidelines. 24 babies showed ROP in various stages among which 6 needed treatment and 18 showed regression of ROP on subsequent follow-up's. The collected data was analysed to know the significance of association of various risk factors to ROP.

KEYWORDS : Retinopathy of prematurity, childhood blindness, ROP screening, risk factors of ROP

INTRODUCTION

Retinopathy of prematurity (ROP) is a disease involving the developing blood vessels of the retina seen in preterm infant. The key pathological feature is the neovascularization of retina which develops in stages from the immature vascular retina of premature infant. ROP is one among the important causes for preventable blindness among children.¹

Because of improved neonatal care and increased survival of low and extremely low birth weight babies, the incidence of ROP is expected to rise increasingly in the near future of developing countries.² Routine evaluation of preterm newborns at risk is not being done at all the places due to a lack of awareness of the disease.³ ROP is a major complication seen in preterms despite the recent advances in neonatal care guidelines and protocols and is considered as a major cause of childhood blindness worldwide.⁴

MATERIALS AND METHODS:

Total of 100 babies were studied who were attending ROP clinic, in Regional eye hospital in Kurnool in the period between November 2019 to October 2021 at Kurnool Medical College and Hospital, were selected according to the inclusion and exclusion criteria -

Inclusion criteria:

- All premature babies (<37 weeks of gestation)
- Low birth weight and other high risk factors

Exclusion criteria:

- Healthy mature babies with birth weight >2500 grams
- Babies with congenital malformations and chromosomal anomalies

Methodology:

Detailed prenatal, natal and antenatal history was noted for all the babies. Birth weight, gestational age and all the relevant risk factors were noted, including oxygen administration, respiratory distress syndrome, blood transfusion, multiple pregnancies, apnea, and mode of birth. Informed consent was taken from the parents or guardians of the babies. Diluted tropicamide (0.5 percent) and phenylephrine (2.5 percent) eye drops were used for the dilatation of pupil. Paracaine is the topical anaesthetic of choice. A sterile eye speculum, an indirect ophthalmoscope with a 20 D lens and a scleral depressor are used to examine the retina. Fundus findings were recorded, including the vascularity of the retina and the zone, stage, and severity of ROP.

Depending on the severity of ROP, babies with an immature retina or any stage of ROP were reviewed for a follow-up examination. Babies who were having stage 3 ROP in zone 2, stage 2 or 3 ROP in zone 1 with plus disease were advised treatment.

RESULTS:

In this study, a total of 100 babies attending regional eye hospital who met the inclusion criteria were examined. 54 were male and 46 were female. Their birth weight ranges from 940 gram to 2300 gram and gestational age at birth ranges from 28 weeks to 36 weeks. Of the examined babies, 17 babies belong to twin gestation. Among them, the other twin was expired for one baby and was not included in the study. ROP was seen in 24 babies among the total 100 babies taken into study. The remaining 76 babies had zone 3A vascularised retina upon 3 subsequent follow ups.

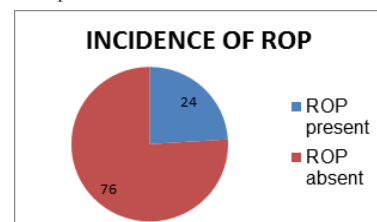


FIGURE 1: Pie-chart showing incidence if ROP

Among the 24 babies with ROP, 11 belonged to zone 2 stage 2 ROP with one of them having plus disease. 4 babies had zone to stage 1 ROP. 3 babies had zone 2 stage 3 ROP with one of them having plus disease. 1 baby belonging to each zone 1 stage 2, zone 1 stage 3, zone 3 stage 1, stage 4A, APROP and hybrid APROP were seen.the management plan followed for each of them is shown in the following table.

TABLE 1: Various stages of ROP seen in the study and the management plan followed

ROP pattern	No. of babies	Advice & final outcome
Zone 1 Stage 2 ROP	01	Follow-up in 1 week Spontaneous regression
Zone 1 Stage 3 ROP	01	Laser photocoagulation
Zone 2 Stage 1 ROP	04	Follow-up in 2 weeks Spontaneous regression

Zone 2 Stage 2 ROP	10	Follow-up in 2 weeks Spontaneous regression
Zone 2 Stage 2 ROP with plus disease	01	Laser photocoagulation
Zone 2 Stage 3 ROP	02	Follow-up in 1 week Spontaneous regression
Zone 2 Stage 3 ROP with plus disease	01	Laser photocoagulation
Zone 3 Stage 1 ROP	01	Follow-up in 2 weeks Spontaneous regression
Stage 4 A ROP	01	Pars plana vitrectomy
APROP	01	Laser photocoagulation
Hybrid APROP	01	Intra vitreal avastin injection

Among the 24 babies with various stages of ROP, 6 required treatment. The other 18 babies were advised frequent follow-up and healthy weight gain. They showed spontaneous regression of ROP on subsequent follow-up visits. Last follow-up visit was at 41 weeks PCA (post-conceptual age). In this study Regressed ROP was seen in 75% of the cases.

Analysis of the various risk factors of ROP was done to know the significance of association of each risk factor to the incidence of ROP. Of the 100 babies taken into study, 24 belonged to early preterm, 44 belonged to intermediate/moderate preterm, 32 belonged to late preterm. The incidence of ROP was 50% in early preterm, 18.18% in intermediate preterm and 12.5% in late preterm. This shows the significantly higher incidence of ROP associated with increasing prematurity.

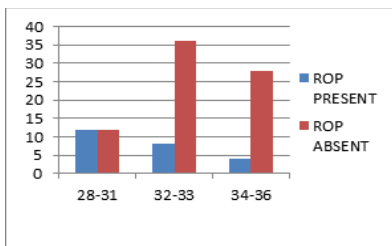


FIGURE 2: Bar diagram showing incidence and association of ROP in relation to gestational age

Of the 100 babies taken into study, 4 babies belonged to extremely low birth weight, 56 babies belonged to very low birth weight and 40 belonged to low birth weight. The incidence of ROP was 75% in ELBW, 26.78% in VLBW and 15% in LBW. This shows that lower is the birth weight, higher is the incidence of ROP

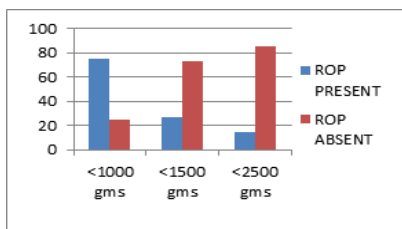


FIGURE 3: Bar diagram showing incidence and association of ROP in relation to birth weight

Evaluation of the other risk factors associated with ROP was done and the frequency of those risk factors in preterm babies with ROP and in those without ROP was calculated and noted. Significantly higher association with ROP is seen with respiratory distress syndrome, oxygen inhalation, anaemia, neonatal jaundice, blood transfusion, exchange transfusion, sepsis, birth asphyxia, apnoea and twin pregnancy. No significantly increased association was seen with intra-uterine growth retardation and cesarean delivery. The following bar diagram shows the presence of each risk factor in the babies under study calculated separately for those with ROP and those without ROP.

FIGURE 4– Frequency distribution of risk factors in preterm babies

with ROP and in those without ROP. (BLUE bar indicates frequency of risk factor in ROP positive babies, RED bar indicates frequency of risk factor in ROP negative babies)

DISCUSSION:

Prematurity, low birth weight and oxygen administration are the most important risk factors in the development of ROP. With increasing neonatal care directed towards improval of survival of preterm babies there is increase in the number of ROP cases seen. Care should be taken in monitoring the amount of oxygen administered to the preterm babies to help prevent the incidence of ROP. The other important risk factors associated with ROP are Respiratory distress syndrome, asphyxia, apnoea, anaemia, blood transfusion, exchange transfusion, sepsis and neonatal jaundice all of which are included in this study.

It is essential to screen all the preterm babies for ROP according to the established guidelines. The follow-up examinations should be planned on the current findings to avoid both, the unnecessary stressful examination due to frequent follow-up in babies who do not have an indication or risk and also to avoid the preventable blindness which can be aided by the early pick-up of disease and early management.

ROP has a biphasic disease process. The hyperoxia induced downregulation of VEGF, resulting in a halt in normal retinal growth and vessel constriction leading vasocessation is the 1st phase of ROP.⁵ The hypoxia in the non-vascularized retina causes up-regulation of VEGF leading to angiogenesis and development of ROP in the 2nd phase of ROP.⁶

ROP is a complex multi-factorial disease. The following are considered to be risk factors for the development of ROP: gestational age, low birth weight, respiratory distress syndrome, apnoea, asphyxia, oxygen therapy, sepsis, anaemia, blood transfusion, exchange transfusion, neonatal jaundice, IUGR, LSCS.⁷

Classification of ROP:

ROP classification as given by ICROP⁸, can be done based on: first, the position of the abnormal vascular development in relation to the optic nerve (zone); second, the degree of abnormality (stage); third, the presence or absence of dilated and tortuous posterior pole vessels (plus disease); fourth, the extent of the disease (clock hours).

Zones:

The retinal vascular development can be described based on the extent into three zones¹⁹.

Zone – 1 : circle drawn on the posterior pole with the optic disc as the centre and the radius that equals twice the distance between the optic disc's centre and the fovea.

Zone - 2 : circle is drawn with the optic disc as the center and the distance from the optic disc center to the nasal ora serrata as the radius, Zone 2 is the area between zone 1 and this boundary.

Zone - 3 : The temporal arc of retina extending beyond the radius of zone 2 is zone 3.

Stages:

To explain the severity of ROP, five stages of abnormal vascular development have been described¹⁹.

- Stage 0: Presence of immature retinal vasculature without any associated pathological changes.
- Stage 1: Presence of a demarcation line separating the posterior vascular retina from the anterior avascular retina. cells) of this cells causes thickening and widening of the line, thus making it visible.
- Stage 2: Charecterised by the presence of ridge i.e, a demarcation line with height, width and volume.
- Stage3: Charecterized by the presence of extraretinal fibrovascular growth along with ridge.
- Stage 4: Characterized by the presence of partial or subtotal retinal detachment.
- Stage 4a – Extrafoveal subtotal retinal detachment.
- Stage4b-Subtotal retinal detachment involving the macula.
- Stage5 :- Total retinal detachment.

Plus Disease:

Increased venous dilatation and arteriolar tortuosity of the posterior

retinal vessels in atleast two quadrants of the eye is described as plus disease.¹⁹

Pre-plus disease:

It is characterised by the presence of abnormal arteriolar tortuosity and venous dilation in the retina of the posterior pole, which is insufficient for diagnosis of plus disease.

Aggressive PosteriorROP(APROP)

This is a severe and rapidly progressive form of ROP characterised by the presence of vascularization that ends in zone 1 or very posterior zone 2, ill-defined peripheral retinopathy and is accompanied by severe plus disease. APROP has the potential to progress rapidly to stage 5 ROP without passing through the other stages.

The 1st screening for preterm neonates should be at four weeks chronologic age (CA) or 31-33 weeks postconceptional age. The further follow-up examinations should be done according to the stage of ROP and zone of vascularisation.

Follow-up in 1 week or less :

- Zone 2 stage 3 and no plus
- Zone 1 stage 1 or 2 and no plus

Follow-up in 1-2 weeks:

- Zone 2, no plus, stage 2
- Zone 1, immature, no ROP
- Zone 1, regressing ROP

Follow-up in 2 weeks:

- Zone 2, stage 1, no plus
- Zone 2, regressing ROP

Follow-up in 2-3 weeks:

- Zone 3, stage 1 or 2, no plus
- Zone 2, immature, no ROP
- Zone 3, regressing ROP

Management is planned according to the stage of ROP.

Ablative laser therapy:

- zone 1, stage 1 to 3 with plus disease
- zone 1, stage 3 without plus disease
- zone 2, stage 2 or 3 with plus disease
- APROP

Vitreoretinal surgical intervention:

- Stage 4 or 5 ROP

CONCLUSION:

Thorough fundus examination involving all the clock hours of retina with indirect ophthalmoscope is important in all preterm babies as a part of screening. RETCAM can be used for screening in remote areas and necessary cases can be considered for expert opinion referral and management.

ROP is a potentially blinding condition which leads to visual impairment and blindness in children. The vision of the high risk newborns can be saved by following these steps :

- Avoiding risk factors
- screening and monitoring of infants with high risk factors on a regular basis.
- early intervention in necessary cases.

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