



RISK FACTOR AND OUTCOME OF RETINOPATHY OF PREMATURITY: A HOSPITAL BASED STUDY

Ophthalmology

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ABSTRACT

Retinopathy of prematurity, is a disease of premature infants born before 31 weeks of gestation. Prematurely born babies receiving high oxygen concentration, followed by sudden withdrawal, causes disorganized growth of retinal vessel and eventually results in retinal detachment and scarring. It may resolve spontaneously or leading to blindness worldwide.

Aim

1. To determine its various clinical risk factors.
2. To determine the outcome of positive cases

Materials and Methods: This hospital based, prospective study was done in Regional Institute of Ophthalmology, Guwahati Medical College and Hospital. A total of 168 eyes of 84 babies were evaluated and the results were statistically analysed. The period of study was from June 2020 to May 2021. The results were statistically analysed using fisher's exact test or chi square test for independence. **Results:** In a total of 84 babies (168 eyes) the risk factors which had significant association with ROP in this study are: Premature new-born, low birth weight, supplemental oxygen, respiratory distress syndrome. In addition, however, risk factors like advanced maternal age, hypertensive disorders of pregnancy, gestational diabetes, premature rupture of membranes and sepsis also show significant association with ROP. All cases of stage1 resolved spontaneously. Of the three cases in stage 2, 2 resolved spontaneously and one had progressed to stage 3.

KEYWORDS

ROP, Oxygen supplementation, Prematurity, respiratory distress syndrome, , intravitreal anti-veg

INTRODUCTION

Retinopathy of prematurity is a disease of premature infants born before 31 weeks of gestation. Prematurely born babies receiving high oxygen concentration, followed by sudden withdrawal, causes disorganized growth of retinal vessel, and eventually results in retinal detachment and scarring. It may resolve spontaneously or leading to blindness worldwide.

Table 1: Staging For The Eye Is Determined By The Most Severe Appearance

Stage 1	Demarcation Line: a flat white line within the plane of retina at the junction of the vascular and avascular retina
Stage 2	Ridge at the junction of the vascular and avascular retina
Stage 3	External fibrovascular proliferation
Stage 4	Subtotal Retinal Detachment
Stage 5	Total Retinal Detachment

MATERIALS AND METHODS

The hospital-based study was done Guwahati Medical College and Hospital. A total of 168 eyes of 84 babies were screened and evaluated and the results were analysed statistically. The study period was from June 2020 to May 2021.

Proper informed consent of the parents and ethical clearance was taken.

Inclusion Criteria

1. All neonates with birth weight less than 2000 grams
2. All neonates with gestational age less than 34 weeks
3. All infants born at > 34 weeks gestational age with associated risk factors like prolonged oxygen requirement; respiratory distress syndrome, sepsis, phototherapy, advanced maternal age, hypertensive disorders of pregnancy, gestational diabetes, premature rupture of membranes.

Tropicamide 0.4% and 1.25% phenylephrine used thrice or more at an interval of 15 minutes for dilatation of pupil till complete mydriasis and examined by indirect ophthalmoscope. The risk factors were analysed statistically using fisher's exact test or chi square test for independence. The p-value less than 0.05 was considered statistically significant.

RESULTS

Sample included a total of 84 babies, out of which 12 babies developed ROP in both eyes i.e., 24 eyes were found to be having ROP.

The mean birth weight of all babies was 1390 grams and that of babies who developed ROP was 1170 grams.

Gestational Age

The mean gestational age in this study was found to be 30.03 weeks. The p value of gestational age was found to be 0.0065 which is highly significant.

Oxygen Supplementation

11 out of 48 babies supplemented with oxygen developed ROP. 1 out of 36 babies developed ROP not supplemented with oxygen. The two-sided P value is 0.0090, considered very significant.

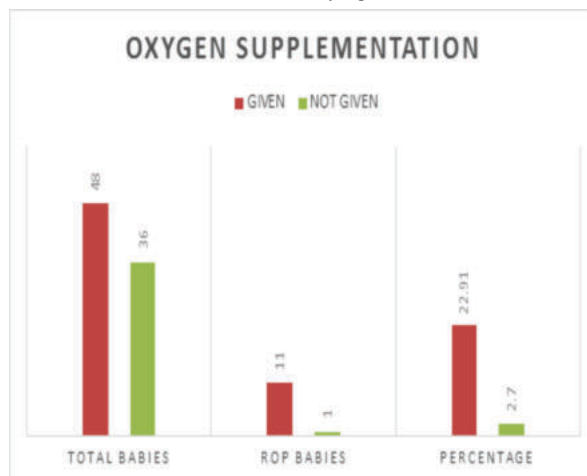


Figure 1: Bar Diagram Showing Oxygen Supplementation.

Respiratory Distress Syndrome (RDS)

9 out of 33 babies having RDS developed ROP while 3 out of 51 without RDS developed ROP. The two-sided P value is 0.0062, considered very significant. Relative risk ratio is 4.63.

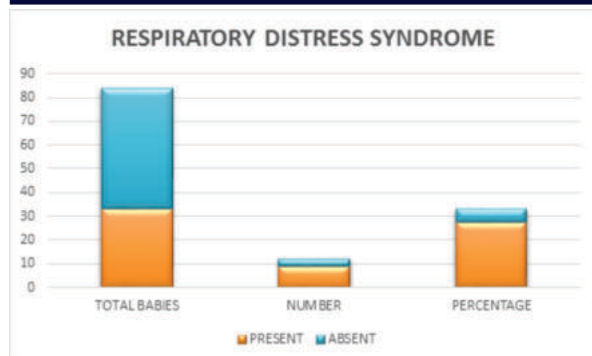


Figure 2: Bar Diagram Showing Respiratory Distress Syndrome

Hyperbilirubinemia

8 out of 34 babies having hyperbilirubinemia developed ROP. 4 out of 50 babies without hyperbilirubinemia developed ROP. The two-sided p value is 0.045, considered marginally significant.

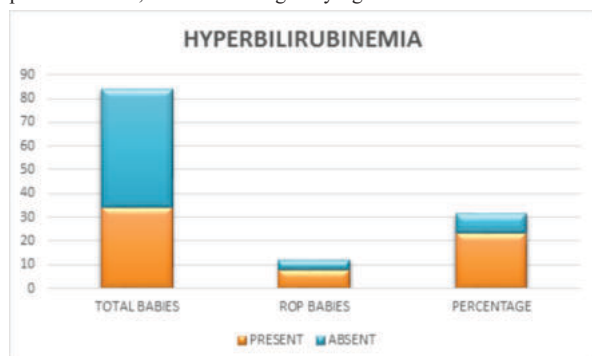


Figure 3: Bar Diagram Showing Hyperbilirubinemia.

Phototherapy

8 out of 32 babies who received phototherapy developed ROP while 4 out of 52 babies developed ROP without phototherapy. The two-sided P value is 0.0277, considered very significant

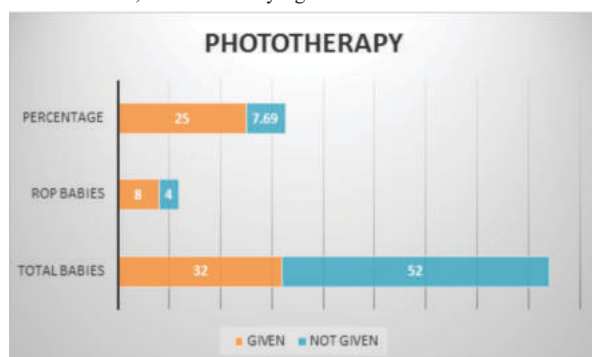


Figure 4: Bar Diagram Showing Distribution Of Phototherapy Among Screened Babies

Gestational Diabetes

4 out of 12 babies of gestational diabetes mother developed ROP while 8 out of 72 babies without GDM mother developed ROP. P value-0.0417 considered marginally significant.

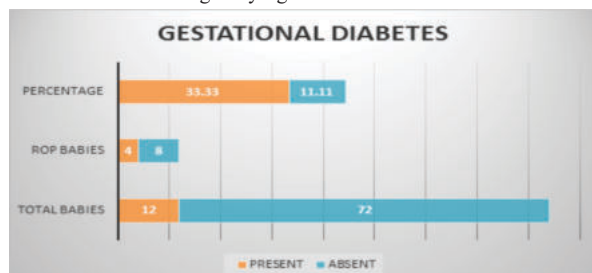


Figure 5: Bar Diagram Showing Distribution Of Gdm In Mothers.

Neonatal Sepsis

7 of 30 neonatal sepsis baby developed ROP while 5 out of 54 without neonatal sepsis developed ROP. The two-sided p value is 0.077, considered marginally significant. Relative Risk ratio is 2.52.

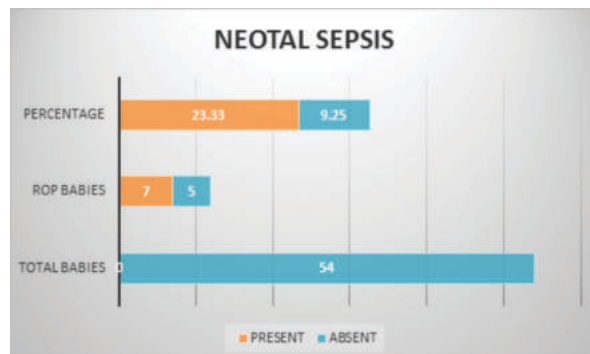


Figure 6: Bar Diagram Showing Distribution Of Neonatal Sepsis Among Screened Babies.

Outcome Of Retinopathy Of Prematurity

Table 2: Showing Stages And Its Zones Of ROP

	Zone 1	Zone 2	Zone 3	Total eyes
Stage 1	0	4	8	12
Stage 2	0	2	4	6
Stage 3	0	2	2	4
Stage 4	0	1	0	1
Stage 5	1	0	0	1
ROP Total	1	9	14	24 eyes

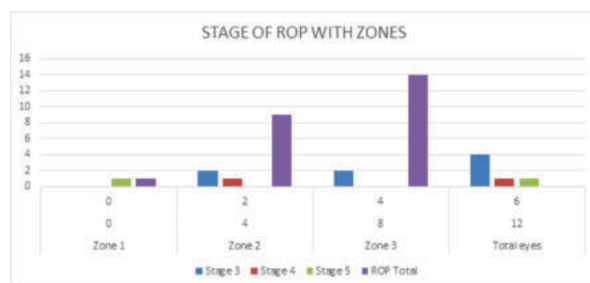


Figure 7: Bar Diagram Showing ROP With Zones

- STAGE 1: total 6 cases were found in stage 1. Out of them, 4 cases were in zones 3 and 2 were in zone 2.
STAGE 1 ZONE 2: On screening, 2 cases were found in stage 1 zone 2. On first follow up one was in stage 1 zone 3 and the other was in the same zone. On the second follow up, both had regressed.
- STAGE 2 ZONE 3: On screening, 3 cases were found in stage 2. On first follow up, 1 case had regressed, 1 was in stage 1 zone 3 and one was in same zone. The case progressed to stage 3 in second follow up and was treated with laser photocoagulation in both eyes following which there was regression. The other two cases regressed spontaneously without any intervention in subsequent follow ups.
- STAGE 3: On screening, 2 cases (4 eyes) were found in stage 3. 2 eyes were treated with confluent laser. 1 eye was given laser followed by anti-vegf and one was given only intravitreal anti-vegf. On first follow up, both cases showed regression to stage 1 zone 3. In second follow up, both cases showed anatomical regression. In third follow up, both cases had regressed.
- Stage 4 and 5: In one case, one eye was in stage 4 (partial retinal detachment) and the other was in stage 5 (total retinal detachment). The case was referred for vitreoretinal surgical correction.

DISCUSSION

In our study, 84 babies fulfilling the inclusion and exclusion criteria were examined.

Incidence of ROP

In the current study, in a total 84 babies (168 eyes) the incidence of ROP was found to be 14.28%

In England, a dataset derived from the National Health Service (NHS) database revealed that 12.6% of babies with birth weight (BW) less than 1500 g had ROP in 2011¹. This is similar to the finding of our study.

In a study by Dwivedi et al² in Madhya Pradesh between 2012-18, the incidence of ROP was found to be 14.2%, which resembles our present study.

Gestational age and birth weight are the two strongest known risk factors for development of ROP. The mean birth weight of all babies who were screened was found to be 1390 grams and that of babies who developed ROP in this study was found to be 1170 grams. The mean gestational age in this study was found to be 30.03 weeks. The p value of gestational age was found to be 0.0065 which is highly significant.

The CRYO-ROP study found that lower birth weight and younger gestational age were strongly associated with developing “threshold” ROP³

The risk factors which had significant association with ROP in this study are:

1. In the present study, oxygen supplementation was found to be a very significant risk factor with p value 0.009 and relative risk factor is 2.54. Pioneering works of Campbell and Ashton explored the role of oxygen in the pathogenesis of a disease of the developing vasculature, retinopathy of prematurity⁴
2. In the present study, RDS has been found to have a very significant association with ROP with p value of 0.0062. A study by Park et al⁵ in South Korea found RDS to be a significant risk factor for ROP with p value 0.008, which resembles our study.
3. The present study has found phototherapy to have a significant association with ROP (p value 0.062)
4. The present study finds sepsis to be a marginally significant risk factor in ROP (p value 0.06).
5. In the present study gestational diabetes is found to be a significant risk factor with p value 0.04.
6. The present study found foetal distress to be only a marginally significant risk factor for ROP.

Not many studies have found foetal distress to be a very significant risk factor.

All cases of stage 1 resolved spontaneously. Of the three cases in stage 2, 2 resolved spontaneously and one had progressed to stage 3. Another 2 new cases (4 eyes) were in stage 3 on screening.

66.6% cases in stage 3 were treated with confluent laser alone following which all cases showed anatomical regression. 16.6% cases in stage 3 required intravitreal anti vegf after laser and 16.6% where laser was not feasible were treated with anti vegf only following which it showed regression in subsequent follow ups.

In present study, 88.8% cases in stage 1 and 2 showed spontaneous regression. Out of total 24 eyes, 16(66.6%) showed spontaneous regression, 25% (6 eyes) required laser photocoagulation with or without anti vegf and 2 eyes in stage 4 and 5 (8.3%) required surgical correction.

The BEAT-ROP trial⁶ elucidated the role of intravitreal ranibizumab in comparison to laser photocoagulation. This study reported a statistically significant reduction in treatment requiring recurrence of ROP in eyes treated with bevacizumab injection as compared with laser ablation.

The CRYO-ROP study⁷ recommended treatment when Stage 3 ROP was present in Zone I or II with plus disease in at least 5 consecutive or 8 cumulative clock hours (thereafter termed “Threshold” ROP).

CONCLUSION

The incidence of Retinopathy of Prematurity in RIO, GMCH in present study (14.28%) is comparable to few studies done worldwide and in India. Nevertheless, it is slightly lower than few recent studies in India, the reason being smaller sample size due to the prevailing covid 19 pandemics at the time of study. The mean birth weight of all screened babies was 1390 grams and mean POG was 30.06 weeks which is comparable to other studies. Significance of risk factors for development of ROP in present study are comparable to other studies, the major risk factors being prematurity, low birth weight, oxygen

supplementation and RDS. In addition, however, risk factors like gestational diabetes, phototherapy and sepsis also show significant association with ROP which is reported only by few other studies only.

6 cases were in stage 1- all regressed

3 cases were in stage 2: 2 regressed in first follow up, 1 had progressed to stage 3 and was treated with confluent laser following which it showed regression

2 cases were found in stage 3: both were treated with laser alone (in 2 eyes) as well as laser followed by intravitreal anti vegf. Both achieved anatomical correction on subsequent follow ups

In one case one eye was in stage 4 (partial retinal detachment) and the other eye was in stage 5 (total retinal detachment). The case was referred for surgical correction.

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