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Original Research Article

Evaluation of Incidence and Associated Risk Factors for Retinopathy of Prematurity: A Prospective Hospital Based Study

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Abstract

Background and Objectives: Increased preterm baby survival rates were facilitated by improvements in neonatal care, which resulted in a rise in the count of children suffering from retinopathy of prematurity (ROP). This study calculated the occurrence of ROP and assesses all possible risk factors.

Study design: Hospital based prospective study.

Setting: Ophthalmology department of Government Medical College and Hospital of south India from March 2012 to August 2013.

Material and Methods: A total of 72 preterm newborns were screened for retinopathy of prematurity between March 2012 and August 2013 after receiving institutional ethical committee permission and the parents' informed written consent.

Outcome measures: The cumulative incidence of ROP was used as the primary outcome measure, while risk factors linked to ROP were used as the secondary outcome measure.

Results: 28 out of the 72 infants who were a part of the study's sample had ROP in some stage in either one or both of their eyes. In the studied population, ROP had an overall incidence rate of 38.89%. There was no statistically significant difference in occurrence between the genders, as calculated by the Chi-square test (P = 0.263). Statistically significant disparity were observed in terms of mean gestational age (29.54±1.78 weeks) and mean birth weight (1030.11±175.07 grams) in the ROP group and control (No ROP) group (32.30±1.82 weeks) and (1371.36±309.63), (P < 0.0001 and P=0.0005, respectively). NICU admission and respiratory distress syndrome also had a significant correlation with ROP (P≤0.01).

Conclusions: Among the population analysed, researchers discovered a striking rate of ROP in this study (38.89%), and the following elements have quite a statistically significant impact on the progress of ROP in its active form: early gestational age, a low birth weight, NICU admission, as well as respiratory distress syndrome (p < 0.05). Ophthalmologist and neonatologist should work together for timely screening and regular follow up to reduce the burden of blindness due to ROP.

Keywords: Preterm infants; Retinopathy of prematurity (ROP); Risk factors; Screening.

Introduction

Retinopathy of prematurity (ROP) is a disorder marked by the growth of aberrant retinal arteries as a result of the retinal tissue's insufficient vascularization brought on by hyperoxia, which causes VEGF to be downregulated and endothelial cells to die. According to this method, VEGF is essential for the endothelium. Retinal tissue that is still developing becomes ischaemic and hypoxic as a result of the closure of developing capillaries. Neovascularization results from this process' upregulation of VEGF [1-3]. Research into ROP has been prioritised on a worldwide scale because of the increased survival rates of very low birth weight premature babies, or those with low birthweight (BW) < 1500 gms, whom are always at risk for developing the disease. The better prenatal care may be responsible for these higher numbers. Due to the increased incidence, additional preterm birth-related comorbidities [4] that have considerable societal repercussions like blindness owing to ROP are occurring much more frequently. Premature births (before 37 weeks of gestation) account for just around 10% among all births globally [5]. According to Blencowe *et al*. [6], ROP causes 32,000 newborns globally to go blind or experience severe vision impairment every year, 10% of whom are born in Latin America and the Caribbean. It was shown that the risk variables linked to ROP varied by area [7]. These discrepancies may be a result of the population's diversity and disparities in newborn care.

The illness ROP is multifactorial [8]. Many studies list a number of risk factors for this illness, some of which might result in severe ROP (BW, GA, supplementary oxygen, extended ventilatory support, Apgar score, pulmonary disorders, anaemia, intraventricular haemorrhage (IVH), necrotizing enterocolitis, septicaemia) [2, 9–13]. Ophthalmologists and neonatologists may undertake meticulous screening, carry out correct diagnoses, and stop the development of the condition with the aid of the recognition of risk factors impeding the advancement of ROP and understanding of its genesis.

Aim and Objectives

This study calculated average incidence of ROP and evaluates all potential risk factors linked to it.

Material and Methods

This was a prospective hospital based study on 72 preterm infants visited for ROP screening in ophthalmology department of a Government Medical College and Hospital of south India from March 2012 to August 2013. The research was accepted by the Ethical Committee and complete informed written consent was acquired from the parents.

Inclusion criteria: Preterm newborns that met either of the following parameters were included in the study:

1. GA ≤ 32 weeks or BW ≤ 1500 g; or
2. GA between 32 and 37 weeks or BW > 1500 g, as well as any of the risk factors listed below respiratory distress syndrome , oxygen treatment, septicaemia, blood transfusions, multiple pregnancies, pregnancy-induced hypertension, anaemia, intraventricular haemorrhage, etc.

Exclusion criteria:

1. Infants who died or lost follow up during the period of the study without the development of ROP or before the complete vascularisation of retina.
2. Infants whose first visit is before or after the study period.
3. Not willing to give consent.

After producing mydriasis by one drop of tropicamide 0.8% eye drops paired with phenylephrine 1% eye drops administered three times in each eye, with a 15-minute gap in between, fundoscopy was carried out by using an indirect ophthalmoscope with a 20

diopter convex lens. An skilled ophthalmologist with expertise in the detection and treatment of paediatric retinal disorders conducted the examination.

The first evaluation was conducted when the babies were between 4 - 6 weeks old. The vascularization of retina and presence of any ROP were noted. If the retina had not been fully vascularized, infants were called for follow up examinations weekly or twice weekly depending on the zone of vascularization. In accordance with the 'International Classification of Retinopathy of Prematurity', each patient was assigned a stage based on the eye that showed the most severe symptoms of ROP during the follow-up examination. [14]. Those who develop ROP were followed up further weekly or twice weekly or even earlier to assess progression or regression of ROP. Those who met the criteria for treatment were referred to higher centre for management. Follow up examinations were done up to complete vascularization of retina of both eyes of the infants.

Statistical Analysis

The statistical analysis was done utilising the SPSS 21.0 software. Simple proportions were used to describe the prevalence rate of ROP. The gestational age & birth weight among two groups were compared using the T-test. For each variable, odds ratios and p-values were determined. Statistical significance was defined as a P value of 0.05 or below.

Results

Out of the 72 infants included in the study, 28 infants developed some stages of ROP in one or both the eyes. Hence the incidence rate of ROP in the study population is 38.89%.

There is no statistically significant relation between ROP and gender in the study (P= 0.263). (Table 1)

Table 1: Gender and ROP

Gender	Male	Female	Total	Odds Ratio	95% CL	P-Value
ROP	19	9	28	0.568	0.211 to 1.530	0.263

Incidence among both the genders was found to be statistically insignificant (P = 0.263). Statistically significant difference was observed in terms of mean gestational age (29.54±1.78 weeks) and mean birth weight (1030.11±175.07 grams) in the ROP group and control (No ROP) group (32.30±1.82 weeks) and (1371.36±309.63). (P < 0.0001) (Table 2)

Table 2: Distribution of Gestational Age (GA) and Birth Weight (BW) between groups

Parameter	ROP (n=28)	No ROP (n=44)	P-Value
Gestational Age (weeks) (Mean±SD)	29.54±1.78	32.30±1.82	<0.0001
Birth Weight (grams) (Mean±SD)	1030.11±175.07	1371.36±309.63	<0.0001

Among other risk factors, NICU admission (P=0.012) and respiratory distress syndrome (P=0.0001) shows a statistically significant relation with ROP. Oxygen therapy is present in 100%infants with ROP. Hence the statistical analysis yields a very high odds ratio. (Table 3**)**

Table 3: Association of other risk factors with ROP

Parameters	Odds Ratio	95% CL	p Value
Oxygen Therapy	1615475515	1.8879 to 576.8361	P = 0.998
Multiple Gestation	1.94	0.6998 to 5.3845	P = 0.2026
PIH	0.53	0.1855 to 1.5111	P = 0.2346
GDM	0.3	0.0596 to 1.5026	P = 0.1428
RDS	14.58	3.7960 to 56.0250	P = 0.0001

NICU Admission	7.43	1.5549 to 35.4902	P = 0.0120
PDA	3.5	0.5962 to 20.5470	P = 0.1654
Apnoea	1.8	0.5860 to 5.5285	P = 0.3046
Bradycardia	0.78	0.0672 to 9.0015	P = 0.8406
IVH	0.78	0.0672 to 9.0015	P = 0.8406
Sepsis	0.77	0.2761 to 2.1661	P = 0.6247
Anaemia	1.2	0.2476 to 5.8153	P = 0.8209

Discussion

According to the majority of researches [16–17], the incidence of ROP in low birth weight infants in India ranges between 38 and 51.9%. Nevertheless, due to differences in the criteria for inclusion and the paucity of a nationally agreed screening standard for ROP, incidences as low as 21.7% [18] and even as high as 71.1% [19] were also recorded. There are a number of ROP studies that have screened infants who were born at a gestational age of 32 weeks or less, or who weighed less than 1500 g at birth (BW) [4, 11]. Nevertheless, we extended the scope of this study by include infants weighted > 1500 g or delivered at or after 32 weeks of gestation who had detectable risk factors. Even though India is a developing nation the overall incidence of ROP in our context has grown equivalent to industrialised countries [20]. This presumably suggests that immaturity & low birth weight could be the most crucial variables associated with the development of ROP. And as far as these conditions are not addressed the incidence rate of ROP may continue to rise. On the other hand these data may also suggest the growing trend of neonatal care in nations such as India as the incidence of ROP as well as the population at risk for having ROP is reliant on the availability, accessibility, and quality of neonatal care. In the present research the rate of therapy needing ROP was 9.7%. This is comparable to previous investigations. Larson *et al* [21] estimated incidence of treatment required ROP as 12.3% in a community based research in 2004.

In our study, there has been no statistically significant association between ROP and gender. This was largely in accordance to Shah *et al* [22]. Where as a strong link between male gender with ROP was observed by Darlow et colleagues [9].

Our study revealed statistically significant correlation of lower gestations and low birth weight to the development of ROP. Numerous studies revealed that gestational age at low birthweight are by far the most major variable related with the development of ROP [23-26].

RDS is one of the important causes which make preterm infants get exposed to therapeutic concentrations of oxygen. In the present study 56.9% infants had history of RDS. All infants with RDS received oxygen therapy. 89.28% of the infants with ROP had a history of RDS. Only three (10.7%) infants with ROP didn't have a history of RDS.

All the infants with ROP had a history of oxygen therapy hence the odds ratio for the association of ROP with oxygen therapy is a very high value. The presence of oxygen therapy in 100% of the infants with ROP indicated a strong association of ROP with oxygen therapy. While in the no ROP group 63.3% infants had exposure to oxygen. In the ROP group, since 89.28% of the infants had a history of RDS, they might had received therapeutic oxygen for a longer duration of time. While in the no ROP group only 36.36% of infants had a history of RDS. As more premature infants frequently develop complications related to prematurity they require NICU admissions and thus NICU admissions also shown a statistical association with the development of ROP. This was in agreement with Lucey JF *et al* and Maheshwari R *et al* [27,28]. In contrast to our results,

Maheswari *et al* [29] and Friling *et al* [30] reported that multiple gestation is also an important factor in the development of ROP.

Limitations of the study

Since this trial was conducted at a tertiary care facility, more at-risk infants were examined. It's possible that this led to a high incidence of ROP. As the majority of the infants in the research came via NICU referrals, the population of our study does not accurately reflect the actual population. Hence, extrapolating the prevalence to the entire population was not possible. Another important bias in present research is infants lost for follow-up. We recommend comparable research with larger sample sizes that take into account preterm neonates not staying in the NICU in order to overcome some of the study's constraints.

Conclusion

The assessment of risk parameters that impacted the development of active ROP indicated that statistically significant effect was seen in case of gestational age, birth weight, and respiratory distress syndrome and NICU hospitalization. Timely screening and follow up is necessary to avoid the blindness caused by ROP. Ophthalmologist should also look for other ocular morbidities associated with ROP like refractive errors, amblyopia , strabismus, and glaucoma and they should monitor the effects of regressed ROP like cicatricial retinal detachment, macular dragging etc . Timely intervention by a retinal specialist is essential in cases requiring treatment.

Recommendations

Our recommendations for screening include:

1. Gestational age at birth ≤33 weeks and or a birth weight of ≤ 1400gms.
2. Premature infants with GA >33 weeks and a birth weight >1400gms may be included if there is history of respiratory distress syndrome or prolonged exposure to therapeutic oxygen.
3. To make sure that all the eligible infants are screened and followed up, initial ROP screening should be done before discharge from hospital whenever possible or should get an appointment for screening before discharge.

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