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Original Research Article

A study of the incidence of retinopathy of prematurity in a tertiary care centre in Karnataka

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ABSTRACT

Background: Retinopathy of prematurity is a preventable cause of childhood blindness. Proper understanding of the classification, risk factors and treatment methods is a must in tackling this disease. The aim of this study was to know the incidence of ROP in preterm infants in a tertiary care centre and to improvise the selection criteria in future in Indian babies.
Methods: A retrospective study of all infants admitted to the NICU from 2016 to 2018 who met the criteria for ROP screening were included in the study. Examination of the eyes was done by a trained technician using a Ret Cam digital imaging in collaboration with KIDROP, Narayana Nethralaya and later interpreted by trained ophthalmologists using the concept of teleopthalmology. Babies were followed up and screened accordingly. Qualified infants were treated with argon laser photocoagulation within 48h of diagnosis. They were followed until the disease was successfully treated.
Results: In current study, incidence of ROP was found to be 10.2%. The gestational age ranged from 28-36 weeks with a mean of 30.5±1.5 weeks. In current study, the most prevalent prenatal risk factor was multiple gestation and postnatal risk factors was anemia, low birth weight ,low gestational age and the use of oxygen therapy.
Conclusions: Screening for ROP, in India, should be performed in all preterm neonates who are born <34 weeks gestation and/or <1800 grams birth weight; as well as in babies 34-36 weeks gestation or 1800-2000 grams birth weight if they have risk factors for ROP.

Keywords: Prematurity, Ret Cam digital imaging, Retinopathy of prematurity

INTRODUCTION

Retinopathy of prematurity (ROP) is a major cause of preventable blindness in children in the developing and developed world despite currently available surgical treatment in late stages of the disease.[1,2] ROP is a vaso-proliferative disorder occurring predominantly in premature infants and typically manifests 3-4 weeks after birth. When normal vasculature of the developing retina is interrupted due to any injury/insult, neovascularization takes place after a latent period. However, if it is abnormal, then it leads to progressive retinopathy, resulting in retinal detachment and blindness. Various risk factors for ROP include prematurity, hyperoxia, hypoxia, hypercarbia, sepsis, apnea and blood transfusions. Recent estimates show that 32,000 infants become blind or visually impaired from ROP every year world- wide, being a far higher estimate than 10 years ago. Most of the ROP blind infants were born in countries in Asia.[3] Approximately 15 million babies are

born preterm worldwide each year and India is the country with the highest number of preterm births.[4]

According to a recent estimate in 2010, 3.5 million infants were born preterm in India. Approximately one in six i.e. 6,00,000 were very preterm i.e. born less at less than 32 weeks gestation age. Assuming 40% of these live born premature infants are admitted to special newborn care units (SNCUs) with 80% survival chances, approximately 1,92,000 infants are at high risk of severe ROP and need to be screened each year. Assuming 5-10% of these survivors develop ROP which needs treatment, which translates to 10,000-20,000 infants a year. This is a minimum estimate, as infants with a gestational age of 32-36 weeks are also at risk of ST-ROP particularly in settings where infants receive less than optimal care. It is estimated that more than 3000 infants become blind or visually impaired from ROP each year due to lack of screening and treatment.

Although ablation treatments can reduce the incidence of blindness by 25% in infants with late-stage disease, the patients often still have poor visual acuity after treatment. Majority of these incidences of blindness, however, were preventable if diagnosed and treated on time before retinal detachment took place. Appropriate screening and timely treatment are important to avoid ROP-induced blindness. Because the ROP screening procedure can cause pain in neonates and has medical costs, appropriate screening criteria should be applied to minimize the number of neonates for screening without missing any type I, ROP that obviates treatment.

While some risk factors like septicemia, blood transfusions, apnea and anemia have been investigated in Indian centres, others like multiple birth, respiratory distress, hyaline membrane disease, jaundice need further study. Similarly, the influences of maternal risk factors also need to be investigated. Moreover, there is a disparity between the profiles of ROP infants in developing countries versus developed countries, and no unified screening guidelines exist for ROP in India. If current American and British screening guidelines for ROP infants were applied in India, a large proportion of Indian infants would be missed because heavier infants (>1500 g) are also at a risk for developing ROP.[5] The purpose of this study was to know the incidence of ROP in our tertiary neonatal unit, the risk factors and their correlation with ROP and to come up with an effective screening protocol for Indian babies.

METHODS

The present retrospective study was conducted in a level 2 neonatal intensive care unit (NICU) at a Government teaching hospital, SIMS in Shivamogga, Karnataka, between April 2016 to February 2018. All the babies admitted during this period meeting the inclusion criteria were included in the study. Sample size was 591. All preterm infants inborn and outborn, admitted in NICU who met the inclusion criteria were screened.

Inclusion criteria

Inclusion criteria for current study were; premature infants admitted with ≤34 weeks gestation and/or birth weight ≤1800 g and babies between 1801-2000 g and/or 34-36 weeks with risk factors for developing ROP like respiratory distress syndrome, sepsis, multiple blood transfusions, multiple births, hyperbilirubinemia.

Exclusion criteria

Exclusion criteria for current study were; parents of babies from whom consent for the study could not be obtained and babies who died before full vascularization of the retina.

Procedure

Gestational age was calculated according to new Ballard scoring system, last menstrual period and antenatal ultrasonography.[6] Relevant patient data (birth weight, sex, gestational age, risk factors, ROP status, and staging) was entered in a pretested proforma. Investigations like sepsis screen, arterial blood gas analysis, or other relevant investigations were done as and when required. Anemia was defined as a hematocrit of <40 and sepsis was defined as clinical and hematological evidence of sepsis (increased or decreased total leucocyte counts, absolute neutrophil count, C-reactive protein, positive blood culture).

Mydriasis was achieved using 1% tropicamide drops.[7] The babies were examined with Ret-Cam digital imaging by a well-trained technician. The Ret-Cam digital imaging system enabled the capture of full colour images of paediatric retina that could be used for immediate assessment of the retina and anterior chamber. Digital images were sent electronically to the ophthalmologist for immediate interpretation and tracked longitudinally over time. ROP status was documented using the International Classification of ROP including stage, zone and extent of disease.[8]

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.

Laser treatment

Laser photocoagulation was advised for infants who developed threshold disease as per ICROP classification or earlier, if aggressive progression was seen in zone 1 disease.[8]

Data analysis

Data analysis was performed using statistical package for social science (SPSS) software version 16 and the results were presented as frequencies and percentages. Chi-square test was used to assess the statistical significance of the association of the factors involved. In the entire test, the p value of less than 0.01 was accepted as indicating statistical significance.

RESULTS

591 babies were screened for ROP in the SNCU from year 2016 to 2018. Their birth weight ranged from 750-2000 g with a mean of 1316±267 g. The gestational age ranged from 28-36 weeks with a mean of 30.5±1.5 weeks. ROP was seen in 60 infants and the overall incidence of ROP was 10.2%. There were 296 males and 295 females and ROP was present in 30 males and 30 females showing no gender predominance.

Table 1: Demographics, incidence, prevalence and treatment outcomes among the study population.

Demographics	ROP present N (%)	ROP absent N (%)	Significance	Required laser treatment
Gender				
Male	30 (10.2)	266 (89.8)	Not Significant	2
Female	30 (10.1)	265 (89.9)		
Gestational age (weeks)				
28-32	46 (14)	283 (86)	p<0.01	2
32-34	12 (6)	194 (94)		
34-36	2 (3.5)	54 (96.4)		
Birth weight (grams)				
750-1000	8 (80)	2 (20)	p<0.01	2
1000-1500	39 (15.4)	213 (84.5)		
1500-2000	13 (4)	306 (95.9)		
>2000	0 (0)	10 (100)		

Table 2: Risk factors for developing ROP.

Risk factors	N	Cases with ROP N (%)	P value
Birth weight <1500 g	262	47 (17.9)	<0.01
Oxygen therapy	289	47 (16.2)	<0.01
Anemia	74	34 (45.9)	<0.01
Sepsis	174	16 (9.2)	0.619
Hyperbilirubinemia	113	6 (5.3)	0.058
Multiple gestation	86	11 (12.7)	<0.01

As the gestational age decreased, the incidence of ROP increased (p<0.01). The incidence of ROP in 10 ELBW infants was 80%, in the 219 VLBW infants, it was 15.4% and was 4.2% in 314 infants weighing 1500-1999 g. No ROP was seen in 10 infants with birth weight above 2000 g and gestational age more than 34 weeks. In current study, incidence of ROP was found to be 10.2%. Out of these, 16.7% had Stage 1 disease, 83.3% had Stage 2 disease. In 58 infants, both eyes were affected. In 2 infants, only one eye (right) was affected. ROP was most commonly seen in zone III (64.6%) and zone II was the second most common (33.4%), 2% in zone 1.

Anemia in babies was found to be a significant risk factor contributing to ROP. In our study 34 babies out of total 74 babies who received blood transfusion developed ROP which was statistically significant with a p<0.01. Anemia may predispose to ROP by producing tissue hypoxia. The most prevalent postnatal risk factors among patients with ROP was the use of oxygen therapy. 78% of patients with ROP needed oxygen therapy. Among 242 babies who received oxygen therapy, 47 babies developed ROP which was statistically significant. Mean duration of oxygen therapy required was 6 days (range: 1-28 days). Multiple gestations were one of the most common prenatal risk factors with a prevalence of 12.8% among infants with ROP which was statistically significant.

In current study, association with other factors like hyperbilirubinemia (p= 0.058) and sepsis (p=0.619) were found to be statistically insignificant (Table 2). Only two babies underwent light amplification by stimulated emission of radiation (LASER) treatment . Complications associated with treatment were minimal.

DISCUSSION

Severe ROP is a debilitating disease, which when left untreated, may lead to blindness, resulting in a poor

quality of life for the individual. It poses a huge financial burden on the individual and the community.[9]

In India, approximately,1 in 1000 children is blind, and the incidence of ROP is reported between 24% and 47%.[10] As per current study the incidence of ROP among preterm infants admitted to NICU was 10.2% which is lower in comparison with Ahuja et al and other studies on ROP in Indian population. Among the Indian studies, Ahuja et al conducted a prospective cohort study in 2018 reported overall incidence as 32.6%.[11] They had studied 325 babies with <36 week gestational age, and the birth weight criteria in their study were <1900 g. The incidence of ROP in their study was low compared to other previous studies in India.[11] The incidence of ROP has shown a declining trend in current study as compared to previous Indian studies which could be due to good antenatal care, obstetric and neonatal care programs in the periphery, awareness about ROP among pediatricians and most importantly availability of expert ophthalmologists through the use of tele-ophthalmology for screening programs.

ROP is a multifactorial disease with risk factors such as low GA, oxygen therapy, sepsis and blood transfusion shown to influence its incidence. Of these low GA (prematurity) continuous oxygen therapy and low birth weight are considered the most important risk factors for ROP. Many ROP studies screened only infants born with less than 32 weeks' gestation or with less than 1500 g of BW.[12,13] In current study, however, we included infants with birth weight less than 1800 g or more than 34 weeks' gestation with determined risk factors associated. As the gestational age decreased, the incidence of ROP increased ($p<0.001$). This was comparable with the previous studies.[12,14] The mean gestational age of the ROP babies was 30.5±1.5 weeks while that of non-ROP babies was 32.5±1.8 weeks which was similar to previous studies.

In current study, low birth weight was identified as a risk factor for ROP. This is in agreement with Hungi et al.[15] The incidence and severity of ROP show an inverse relationship with BW and GA, with few cases diagnosed in babies weighing over 1500 g or babies whose GA is >32 weeks at birth.[16] The incidence of ROP in our study in ELBW infants was 80%, 18.5% in the VLBW infants, it was and was 4.1% in infants weighing 1500-1999 g. No ROP was seen in 10 infants with birth weight above 2000 g and gestational age more than 36 weeks. There have, however, been several reports of ROP in bigger and more mature babies in India.[15,17] The low incidence in ELBW babies in our study may be attributed to the decreased survival of the neonates in our SNCU. Our data demonstrate that if the American guidelines were to be used among the Indian population, many ROP cases would remain undiagnosed and hence there is a need for development of specific guidelines for Indian population.

The causal link between ROP and supplemental oxygen has been confirmed by various studies in India and abroad.[18] In current study, preterm babies who received oxygen therapy were found to be more prone to developing ROP. Kong et al 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. We found the incidence of ROP among multiple gestations to be 12.8% which was significant but was lower when compared to other studies.[19] A larger sample size of preterms resulting from multiple gestations needs to be done to confirm this hypothesis. Other postnatal risk factors studied were presence of sepsis (10.6%), apnea of prematurity (8%), blood transfusion (9.9%), hyperbilirubinemia (11.3%) which were not significant. Only two babies underwent LASER photo coagulation, both the babies were extremely low birth weight male babies with an average gestational age of 28 weeks. Both the babies required oxygen therapy, respiratory support, had sepsis and underwent blood transfusion. Complications associated with the treatment however were minimal.

Limitations

A limitation of current study was the decreased survival of ELBW babies in our NICU which may have accounted for the relatively low incidence of ROP in current study.

CONCLUSION

India has the highest number of preterm deliveries in the world and hence, a huge burden of ROP. Current study outlines the prevalence of pre and postnatal risk factors for the development of ROP and highlights the need to develop refined screening guidelines to better assess the Indian population. The data collected from this study should be combined with other studies of ROP in India to help construct and validate a unified screening protocol. We recommend screening infants ≤34 weeks of gestation and infants born ≤1800 g birth weight in India as larger babies were also found to have ROP in our country. We also stress the importance of following strict oxygen therapy guidelines and transfusion practices in the NICU to decrease the incidence of ROP.

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