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Original Research Article

Retinopathy of prematurity: study of incidence, risk factors and outcome in level 3 neonatal intensive care unit in a tertiary care centre

Uma Devi Rachamadugu, Sravani Devana, Srikanth Sandanala*

Department of Pediatrics, Gandhi Medical College, Secunderabad, Telangana, India

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***Correspondence:**
Dr. Srikanth Sandanala,
E-mail: dr.srilu84@gmail.com

ABSTRACT

Background: Advancing technology in antenatal and neonatal care has resulted in better survival of preterm neonates in developing countries in the past few decades. This has resulted in an apparent increase in the incidence of Retinopathy of Prematurity (ROP), which is the most important cause of preventable blindness in infants.
Methods: A prospective clinical study was done for 18 months in 400 preterm babies less than 34 weeks of Gestational Age (GA) or less than 1750 gm of Birth Weight (BW). ROP screening was performed. The babies who developed any stage of ROP were taken as cases and the babies who did not have ROP were taken as controls. Statistical analysis was performed using SPSS software (Version 20.0). p value <0.05 was taken as statistically significant.
Results: Four hundred babies were thus examined. The overall incidence of ROP in the study group was 10.25% (41 babies). Out of them, 38 babies (92.6%) had stage-1 ROP and 3 babies (7.31%) had stage-2 ROP. three babies (7.31%) required laser treatment. Risk factor analysis revealed that gestational age at birth, low birth weight, need for oxygenation, RDS, clinical sepsis, HIE, AKI, NNS, resuscitation, apnea.
Conclusions: Screening should be intensified in the presence of risk factors like resuscitation, oxygen requirement, apnoea and prolonged hospital stay, which can reduce the incidence of severe stages of ROP as shown by this study.

Keywords: Birth weight, Gestational age, Retinopathy of Prematurity, Retinopathy of prematurity screening, Risk factors of retinopathy of prematurity

INTRODUCTION

Retinopathy of Prematurity (ROP), which was previously called as Retrolental Fibroplasia (RFL), is a vaso-proliferative disorder of the retina. Preterm infants are more prone for this disease especially Low Birth Weight (LBW) neonates who are exposed to large amount of oxygen (O_2). It is the major cause of preventable blindness in children in the world. The World Health Organization (WHO) programme of Vision 2020 targeted against ROP mentioned that the incidence of ROP can be reduced by early screening and referral for Treatment.[1] Spectrum of ROP is broad and ranges from a spontaneously recovering stage to a vision threatening sequelae. In infants with Birth Weight (BW) less than 1000 grams, the risk of ROP is 82%, and 9.3% of them are potentially under the risk of blindness.[2] Initially there was a low incidence of ROP in developing countries like India because there was no adequate screening and reporting and there was inadequate awareness regarding the grave consequences of the disease. But now there is an apparently increasing incidence with better screening protocols, more availability of assisted ventilation services and increased survival of preterm in newborn units.[3] The pathogenic process involved in causation of ROP is multifactorial. It is attributed to many possible risk factors like prematurity, hyperoxia, sepsis, necrotizing enterocolitis, intraventricular hemorrhage

(IVH), Low Birth Weight (LBW), prolonged exposure to O2, severity of neonatal illnesses, severe respiratory distress requiring mechanical ventilation, shock, hypoxia, prolonged ventilatory support, need for blood transfusion, acidosis, anemia.[4,5]

The aims and objectives of the study is to know the incidence, Risk factors and outcome of Retinopathy of Prematurity in all neonates less than 34 weeks of gestation admitted in NICU/SNCU of Gandhi Hospital/ Gandhi Medical College, Secunderabad/Telangana, India.

METHODS

The prospective observational study was conducted in NICU, department of pediatrics, Gandhi hospital, Secunderabad, Telangana state. The duration of study is 18months from august 2017 to December 2018. Inclusion criteria included gestational age of less than or equal to 34 weeks with birth weight less than or equal to 1750 gm. The study was done by performing ROP screening in these babies, staging the disease and documenting the risk factors. All the enrolled infants underwent pupillary dilatation with 0.2% tropicamide and 1.25% phenylephrine eye drops, instilled every ten minutes for three applications. Examination was performed by indirect ophthalmoscopy with 20 diopters lens 30 to 40 minutes later. The first screening was performed three to four weeks postnatal depending upon the status of the babies. The follow-up examinations were based on initial findings. After that they were followed until full vascularization of the retina had reached zone 3 or until full remission of ROP, after treatment and diode laser photocoagulation of the peripheral avascular retina. Classification of ROP was done according to the international classification of ROP (ICROP) depending on the severity as stage 1-5.

RESULTS

The present study was conducted in NICU of Gandhi hospital attached to Gandhi medical college and research center, secunderabad from august 2017 to November 2018 of the total admissions to NICU 400 babies satisfy inclusion criteria during the period of study and were screened. Neonates who developed any stage of ROP were considered as cases and the neonates without ROP were considered as controls.

Among 400 babies who were screened 41 babies had retinopathy of prematurity. incidence of ROP in present study was 10.25% among the 41 ROP positive babies 3 cases had stage 2 ROP and 38 cases had stage 1 ROP. 75.60% among cases and 79.66% among controls were delivered vaginally. 24.39% among cases and 20.33% among controlled were delivered by LSCS. There was no difference in the distribution of delivery among cases and controls. p value =0.6866. Among 41 ROP positive cases, one case (2.43%) weighed <1000 gms and 16 cases (39.02%) birth weight ranging between 1001 to 1500 gms and for 24 babies (58.53%) birth weight ranging between 1501 gms to 1750 gms. maximum number of cases and controls had birth weight ranging between 1501 to 1750 gms. Lewis significantly associated with increase of ROP, p value <0.0001. The GA ranged between 27 to 34 wks. among cases and controls. Of the total number of ropcases maximum (63.41%) was among babies born with GA between 29 to 32 wks. whereas for controls maximum (83.84%) were among 32 to 34 wks, which was very significant (p value <0.0001). 27 ROP positive cases required oxygen support, compared to 85 ROP negative cases which required oxygen support which was very significant. 65.85% cases had respiratory distress syndrome compared to 23.67% among controls, which was very significant p value <0.0001. 68.25% of cases had clinical sepsis compared to 45.96% of controls, which was very significant p value 0.001. 65.85% of cases had hypoxic ischemic encephalopathy compared to 23.39% of controls which was very significant value <0.0001. Acute kidney injury was considered in the study group if oliguria (urine output <1 ml/kg) is present and/or if serum creatinine was elevated 2 standard deviation above the mean value for gestational age or rise in value was ≥0.3 mg/dl/day. 21.95% cases had acute kidney injury compared to 5.84% of controls which was very significant. p value 0.0007. 17.07% of cases had neonatal seizures compared to 3.62% of controls, which was very significant. 51.21% cases required resuscitative measures after birth compared to 20.05% controls which was very significant. p value 0.0006. 21.21% cases had apneic episodes compared to 20.05% controls which was very significant. 17.07% of cases had neonatal seizures compared to 3.62% of controls, which was very significant.

DISCUSSION

Significance of ROP screening lies in the fact that ROP is the most common cause of childhood blindness which is preventable. The primary prevention of ROP can be done by limiting the exposure to antenatal, natal and postnatal risk factors which are proposed to contribute to the increased incidence as well as severity of ROP. Secondary prevention of ROP is done by timely screening and early treatment to prevent blindness that can occur in severe ROP who miss the screening and are not treated. So, the secondary prevention of ROP is given utmost importance in the WHO VISION 2020 programme.[6] In this era of improving standards of neonatal care, ROP is becoming a significant problem in developing countries like India. Though there are data from the different urban and rural areas of India, reports from large randomized multicentric trials is lacking from this country. So, there is a scarcity of data on the epidemiology of ROP from the Indian subcontinent.[7] Studies from developed countries have reported that although the clinical spectrum and incidence of ROP is not similar in all the units, there is an overall decrease in the incidence of the disease wherever there is an ongoing surveillance programme.[8] So timely screening is a very important aspect in management of ROP.

Incidence of ROP

The incidence of ROP in the present study is 10.25% Various studies have shown that about 9.4%-25.4% of babies with gestational age 32 wk. or less develop some degree of ROP. Studies in the literature usually use a cut-off point of a BW of 1,250 gm or 1,500 gm or 1,750 gm, a GA of 28 wk. or 32 wks., or both. Using a BW of 1750 gm or less, a GA of 34 wk. or less, or both as criteria for inclusion in this study explains the similar incidence of ROP when compared to other Indian studies. The overall incidence of ROP in the present study is 10.25%. Patil et al, reported the overall incidence of ROP as 17.5% and there was no case of severe ROP.[9] they studied 40 babies with <32 wk. or < 1250 gm. Maheshwari et al, in 1996 reported overall incidence as 20% and severe ROP as 7%. They studied 66 babies with <35 wk. or <1500 gm. Dutta et al, screened 108 babies of ≤32 wk. or ≤1700 gm and reported overall incidence as 21%.[10]

However, in most instances it is not possible to compare studies, as the inclusion criteria are different. The incidence of ROP in this study would have increased if the screening was done only in babies weighing <1300 gm or in babies <32 wk. of GA at birth. Screening of babies with a GA of <34 wk. and/or <1750 gm BW in this study have made the incidence of ROP comparable to other Indian studied. Inclusion criteria of ROP Screening if changed to lower limit of GA or BW (≤30 wk. and ≤1250 gm) would make screening more cost effective and detect the more severe stages of ROP easily enough to permit treatment, reduce unnecessary examinations and avoid wastage of time and manpower. But there are high chances of missing ROP cases which can lead to sequelae which are avoidable with screening and early treatment.

Severity of ROP

Most of the studies consider stage 3 and above as severe ROP. The percentage of severe ROP among various stages of ROP is depicted in the box below. In this study there were no stages of ROP above stage 2, which was similar to study conducted by Patil et al. This could be explained by the fact that the screening programme and surveillance for the risk factors was good in this hospital.

Significant risk factors in various studies

Though accumulating evidence indicates that ROP is a multifactorial disease, immaturity of retina and a period of hyperoxia are the main contributing etiological factors in the pathophysiology of ROP. In this study, the incidence of ROP was significantly inversely proportional to both birth weight (p=0.05) and gestational age (p<0.001) On univariate analysis, the duration of oxygen administration, need for oxygen supplementation, clinical sepsis, apnea, RDS, HIE, acute kidney injury, convulsions, positive CRP, administration of blood and its products and hypotension are significantly associated with development of ROP.

Low birth weight and prematurity

The prevalence of ROP was more among VLBW neonates and the risk is inversely proportional to BW and GA in studies conducted by Maheshwari et al. The mean gestational age of the cases was 29.93±2.18wk and the controls were 32.42wk±0.89wk. The range of gestational age was 27 wks-34wks among cases and 29wk-34wk among controls. Mean birth weight of the ROP cases were 1340 gms and non ROP babies was 1480 gms. Incidence and severity of ROP increased as the birth weight decreased.

Oxygen administration

The duration of oxygen administered was an independent risk factor for development of ROP (p=0.005). 66.6% of babies who received oxygen therapy developed ROP in the present study and nearly 50 %of the babies on oxygen therapy developed the disease in other studies. Though cases were exposed to hyperoxia and hypoxia more than the controls, it was not found to be a significant factor in causing ROP. This can be explained due to the close monitoring of babies on oxygen therapy by pulse oximetry and arterial blood gas analysis in this unit. The causal link between ROP and supplemental oxygen has been confirmed by controlled trials and clinical studies. However, a safe level of oxygen usage has not been defined. Preliminary work has suggested that continuous oxygen monitoring may reduce the incidence of ROP. In present study oxygen administration is a significant risk factor for development of ROP but not an independent risk factor on multivariate analysis.

Antenatal maternal steroid intake

A study conducted by Rosemary et al, showed that antenatal steroid administration by the mother had a protective effect against ROP in the neonates.[4] But in this study it was not a significant risk factor

RDS

RDS is significant risk factor in the present study but not an independent risk factor on multivariate analysis. Gupta et al, and associates reported ROP in 33.3% of babies with RDS. In this study, 40% of babies among cases had RDS, which is almost comparable to the other studies mentioned. RDS is significant risk factor in the present study but not an independent risk factor on multivariate analysis. Gupta et al, and associates reported ROP in 33.3% of babies with RDS. In this study, 40% of babies among cases had RDS, which is almost comparable to the other studies mentioned.

Sepsis

Clinical Sepsis is an independent risk factor for ROP in the present study (p=0.001) and corroborates with findings of other studies. Gupta et al in his study reported 52% sepsis

among babies with ROP. In the present study clinical sepsis was a risk factor on univariate analysis and 70.37% of the cases had clinical sepsis, but it was not an independent risk factor on multivariate analysis. Its prevention and early treatment may reduce the incidence of ROP. The risk of ROP was independently proportional to the presence of bacterial and fungal sepsis only in ELBW babies and those with threshold ROP in the study conducted by Vikek and associates.[11] But in this study, culture proven sepsis was not an independent risk factor of ROP.

Apnea

ROP is known to be associated with apnea. The number of episodes of apnea was a risk factor on univariate analysis and presence of apnea was an independent risk factor for ROP on multivariate analysis. This can be compared to 54.1% and 54.5% as reported by Agarwal and Gupta respectively. Appropriate management of apnea may reduce the incidence of ROP. Apnea was also found to a risk factor for ROP in studies conducted by Shohat et al, and Gunn and coworkers.[12]

Multivariate analysis of the risk factors

In study conducted by Chaudhari et al, septicemia ($p<0.001$), apnea ($p=0.0001$) and oxygen therapy ($p=0.031$) were independent risk factors In our study on multivariate analysis, GA, duration of hospital stay, day of establishment of feeds, apnea, need for resuscitation and duration of oxygen administration were found to be independently significant risk factors.

CONCLUSION

The incidence of ROP in this study is 10.25%. 38 babies (92.6%) had stage-1 ROP and 3 babies (7.31%) had stage-2 ROP. The birth weight of the ROP babies ranged from 900gm-1700gm (mean 1340±220 gm), while that of non-ROP babies ranged from 1100gm-1750 gm (mean 1480±160 gm). Lower birth weight was significantly associated with increased incidence. The mean gestational age of the cases was 29.93±2.18wk and the controls were 32.42±0.89wk. Low GA is an independent risk factor for ROP. Low birth weight and prematurity are important risk factors for ROP. On univariate analysis, the duration of oxygen administration, mean of maximum and minimum SpO^2, need for oxygen supplementation, clinical sepsis, apnoea, RDS, hypoxic ischemic encephalopathy, acute kidney injury, convulsions. On multivariate analysis by application of multiple logistic regression models, GA, duration of hospital stays, apnoea, need for resuscitation and duration of oxygen administration were found to be independent risk factors. Meticulous fundus examination with indirect ophthalmoscopy should be done in all preterm babies as per the guidelines and screening should be intensified in the presence of factors like apnoea, need for resuscitation, oxygen administration, clinical sepsis, RDS, hypoxic ischemic encephalopathy, acute kidney injury, convulsions, clinical sepsis, positive CRP.

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