

Original Research Article

Anemia in relation to severity of retinopathy of prematurity in preterm babies born in tertiary care centre in South India

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ABSTRACT

Background: Retinopathy of prematurity (ROP) is a vaso proliferative disorder of retina among preterm infants. Significant cause of blindness in children with increased survival of premature infants with improved neonatal care. Potential risk factors for development of ROP include low gestational age, low birth weight, bronchopulmonary dysplasia, sepsis, acidosis, oxygen therapy. Anemia as a cause for retinopathy of prematurity has been postulated but there are very few studies addressed the effect of anemia on incidence and severity of ROP. The objective of this study was to determine the effect of anemia on incidence and severity of retinopathy of prematurity and to determine other factors associated with development of retinopathy of prematurity.

Methods: Retrospective descriptive study of 120 babies born premature less than 34 weeks for the development of Retinopathy of prematurity and its severity and for associated conditions. All babies screened for retinopathy of prematurity at 3 weeks of age and further followed up for progression of ROP. Factors analysed included hemoglobin levels at 3 weeks of life, number of blood transfusions, days on ventilator, gestational age, birth weight, duration of oxygen requirement, bronchopulmonary dysplasia for the development of retinopathy of prematurity. Findings described in simple descriptive manner.

Results: Anemia and increased requirement for blood transfusion are associated with higher incidence and severity of ROP. Low gestational age, birth weight, prolonged oxygen requirement, intraventricular hemorrhage (IVH), sepsis are other risk factors.

Conclusions: It is significant to screen preterm babies for ROP and to anticipate in the background of these risk factors. Minimise oxygen duration and blood loss for sampling to prevent anemia and reduce transfusions.

Keywords: Anemia, Blood transfusion, Prematurity, Retinopathy

INTRODUCTION

Retinopathy of prematurity (ROP) is a disease of developing retinal vasculature, vaso proliferative disorder of retina among preterm infants. Neonates born preterm particularly less than 32 weeks of gestation are at risk of retinopathy of prematurity. It can occur in neonates born later than 32 weeks of gestation if required turbulent NICU course or those requiring prolonged oxygen therapy.¹ Retinopathy of prematurity (ROP) is significant cause of blindness in children with increased survival of

premature infants with improved neonatal care. It is important public health problem in middle income countries due to lack of resources to screen babies for and treat ROP are lacking.² Retinopathy of prematurity develops due to poor retinal vascularization leading to retinal hypoxia and pathological neovascularization. International classification of ROP (ICROP) is used for classifying ROP.³ Classifies ROP based on location, severity, extent. Severity ranges from Stage 1 to Stage 5 which is complete retinal detachment. Location into 3 zones. Extent based on clock hours involved. ROP begins

at 31-33 weeks of post menstrual age with progression during next 2 to 5 weeks. Spontaneous regression can occur in stage 1, stage 2 and early stage 3.⁴ Progression can result in blindness, severe visual impairment. Potential risk factors for development of ROP include low gestational age, low birth weight, bronchopulmonary dysplasia, sepsis, acidosis, oxygen therapy, hyperoxia, hypocarbia, hypoxia, maternal use of beta blockers. Anemia as a cause for retinopathy of prematurity has been postulated but there are very few studies addressed the effect of anemia on incidence and severity of ROP. Greater frequency of blood transfusion as a risk factor for the development of retinopathy of prematurity has been found in some of the studies.⁵ The aim of this study was to determine the effect of anemia on incidence and severity of retinopathy of prematurity and to determine other factors associated with development of Retinopathy of prematurity

METHODS

Retrospective descriptive study in a tertiary care centre lourdes hospital in Kochi, South India. Retrospective analysis of data of 120 babies born premature less than 34 weeks for the development of Retinopathy of prematurity and its severity and for associated conditions. Study duration of 2 years between July 2017-August 2019. Factors analysed included Hemoglobin levels at 3 weeks of life, Number of blood transfusions, days on ventilator, gestational age, birth weight, duration of oxygen requirement, bronchopulmonary dysplasia for the development of Retinopathy of prematurity. All babies screened for Retinopathy of prematurity at 3 weeks of age and further followed up for progression of ROP. Babies were grouped into those with no retinopathy of prematurity, with stage 1 ROP and those with stage 2 and above were clubbed into a single group. Other factors analysed included association of sepsis, Intraventricular hemorrhage, hypoglycemia with retinopathy of prematurity. Findings described in simple descriptive manner. All data analysed retrospectively not involving any ethical issues. SPSS version 20 was used for statistical analysis. Qualitative (categorical) variables were represented by frequency and percentage analysis. Quantitative (continuous/score) variables were represented by mean and standard deviation. Multinomial logistic regression was performed to find the association between ROP and other variables. A p-value less than 0.05 is taken as statistically significant. Selection criteria for babies.

Inclusion criteria

All preterm babies born less than 34 weeks of gestation.

Exclusion criteria

Babies with congenital anomalies and babies requiring exchange transfusion for hyperbilirubinemia.

RESULTS

In this study Incidence of ROP in the study group was 48%. ROP was higher in babies in 23-26 weeks of gestation compared to babies born 26-30 weeks of gestation or higher. 62% babies born at 23-26 weeks of gestation had stage 2 ROP, 32.4% had stage 3 or higher and 5.6% had stage 1 ROP, 40.2% of babies in 26-30 weeks of gestation had stage 2 ROP, 15.4% had stage 3 or higher and 3.7% stage 1 ROP, 20% of babies in 30-34 weeks of gestation had stage 2 ROP, 5% had stage 3 or higher, 7.1% of stage 1. Analysis showed significant correlation between decrease in gestational age with incidence and severity of ROP with a p-value of less than 0.05, 72.8% babies with birth weight of less than 600gms had stage 2 ROP, 27% had stage 3 and above, 53% in 600gms to 1kg birth weight group had stage 2 ROP, 12% had stage 3 or higher, 4.7% with stage 1 ROP. In babies with more than 1 kg birth weight 25% had stage 2 ROP, 10% had stage 3 or higher and 5% stage 1 ROP. Significant correlation between decrease in birth weight with incidence and severity of ROP with a p-value of less than 0.05. Incidence and severity of ROP in babies with anemia at 3 weeks of life was higher in those with severe anemia. 95.8% in babies with Hb <8 mg/dl had stage 2 or higher ROP, 78.9% in babies with 8-10 mg/dl, only 28.1% in babies with Hb >10 mg/dl. 8.8% of babies with Hb >10 had stage 1 ROP (Figure 1).

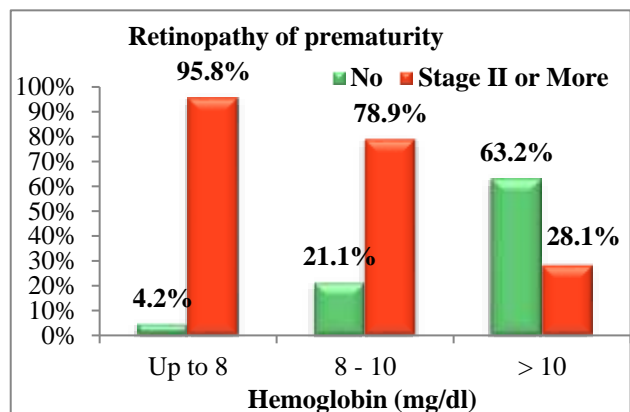


Figure 1: Retinopathy of prematurity and hemoglobin.

Significant association between retinopathy of prematurity and anemia. Analyzing correlation between number of blood transfusion with incidence and severity of ROP, stage II or more of ROP is significantly higher in cases with more than 4 blood transfusions (80.0%) and 2-4 blood transfusions (96.0%) compared to the cases with 0-1 blood transfusions (37.1%) (Figure 2). All babies requiring more than 7 days of mechanical ventilation had ROP of stage 2 or higher as compared to 63.6% of babies requiring 3 to 7 days of mechanical ventilation and 38.7% in those requiring less than 3 days of mechanical ventilation. 8.1% of babies requiring less than 3 days of mechanical ventilation had milder stage1 ROP. Based on duration of oxygen requirement and incidence and

severity of ROP showed that 94.4% of babies requiring more than 21 days on oxygen had stage 2 or more ROP, 75% in those requiring 14-21 days of oxygen, 56.3% in 8-14 days group, 33.3% in babies requiring 4-7 days of oxygen, 18.5% in those requiring 0-3 days of oxygen. 9% of babies had milder stage 1 ROP in 4-7 days group and 3.7% in 0-3 days group. Association between retinopathy of prematurity and days of oxygen requirement is significant with p-value less than 0.05 (Figure 3). Stage II or more is significantly higher in cases with bronchopulmonary dysplasia (95.5%) compared to the cases with no bronchopulmonary dysplasia (42.3%). Stage II or more is significantly higher in cases with sepsis (67.1%) compared to the cases with no sepsis (12.5%). 38% of those with ROP required laser treatment. Stage II or more is significantly higher in cases with shock (66.7%) compared to the cases with no shock (29.4%). Association between retinopathy of prematurity and intraventricular hemorrhage is significant. Stage II or more is significantly higher in cases with intraventricular hemorrhage (82.6%) compared to the cases with no intraventricular hemorrhage (45.5%).

DISCUSSION

In this study 120 babies born preterm less than 34 weeks were studied for the development of retinopathy of prematurity. Babies were screened for retinopathy of prematurity at 3 weeks of life and risk factors analysed for ROP including gestational age, birth weight, Anemia at 3 weeks, requirement of blood transfusions, days on mechanical ventilator and requiring supplemental oxygen. Other factors also analysed included association of Intraventricular hemorrhage, sepsis, BPD with incidence and severity of ROP. Incidence of ROP was 48% which was similar to reports from other parts of India between 20-51.9%.^{6,7} 18% of preterm babies were from 23-26 weeks gestation, 54% from 26-30 weeks of gestation, 28% from 30-34 weeks of gestation. 62% babies born at 23-26 weeks of gestation had stage 2 ROP, 32.4% had stage 3 or higher and 5.6% had stage 1 ROP, 40.2% of babies in 26-30 weeks of gestation had stage 2 ROP, 15.4% had stage 3 or higher and 3.7% stage 1 ROP, 20% of babies in 30-34 weeks of gestation had stage 2 ROP, 5% had stage 3 or higher, 7.1% of stage 1. Incidence of ROP in less than 26 weeks gestation was 77.9% in study by Mitsiakos et al this variation can be due to increased survival of extremely preterm babies but associated with increased incidence of Retinopathy of prematurity.⁸ Incidence and severity of ROP with birth weight, 9% babies were below 600grams, 43% between 600 grams and 1kg, 48% were above 1 kg. 72.8% babies with birth weight of less than 600gms had stage 2 ROP, 27% had stage 3 and above, 53% in 600gms to 1kg birth weight group had stage 2 ROP, 12% had stage 3 or higher, 4.7% with stage 1 ROP. In babies with more than 1 kg birth weight 25% had stage 2 ROP, 10% had stage 3 or higher and 5% stage 1 ROP. The data was comparable to the study by Hwang et al.⁹ It showed incidence of any ROP 76.9% in <500 grams, 83.3% among 500-749grams, 54% in 750-999 grams. Incidence and severity of ROP was higher in babies with Extremely low birth weight similar to study in other parts of India.¹⁰ Evaluating incidence and severity of anemia on ROP, 24% babies had Hb <8 mg/dl, 19% had between 8-10 mg/dl, 57% babies had Hb>10 mg/dl. 95.8% babies with severe anemia (<8 mg/dl) had stage 2 or higher of ROP, 78.9% of babies with Hb 8-10 mg/dl had grade 2 or higher ROP while only 28.1% of babies belonging to >10 mg/dl group. This shows higher incidence and severity of ROP in anemic babies which is similar to results in other studies in India.¹¹ There are conflicting reports related to anemia and retinopathy of prematurity. Study by Bossi et al showed no relation with Hb levels and any stage of ROP and study by Englert JA et al showed higher incidence and severity with duration of anemia.^{5,12} Huang et al anemia as a risk for decreased involution of ROP.¹³ Incidence and severity of ROP with number of blood transfusion, 70% babies required number or 1 blood transfusion, 25% required 2-4 blood transfusions, 5% babies required more than 4 transfusions. Incidence and severity of ROP was higher in group with more transfusions. 80% of babies with >4 transfusions and

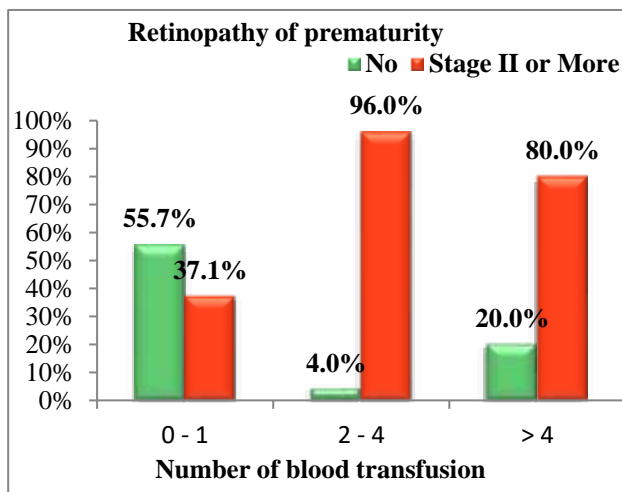


Figure 2: Retinopathy of prematurity and number of blood transfusion.

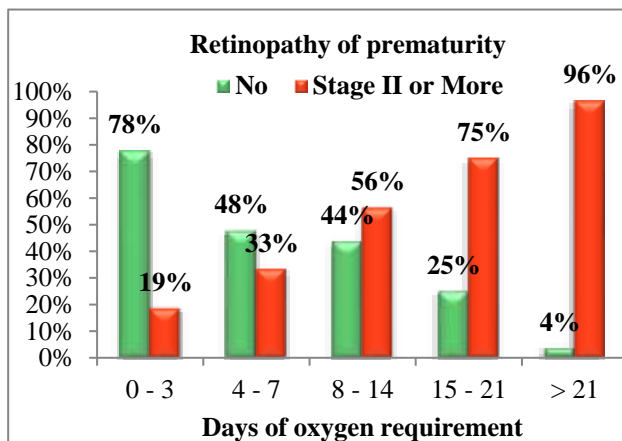


Figure 3: Retinopathy of prematurity and days of oxygen requirement.

96% in those with 2-4 transfusions had stage 2 or higher ROP compared to 37.1% of babies with 0-1 transfusions. This was in accordance with other studies which has higher incidence and severity with increasing transfusions.¹⁴ Study by Dani et al blood transfusion as an independent risk factor for ROP.¹⁵ There are studies which provide no relation with blood transfusion and severity of ROP.¹⁶ ROP in relation to number of mechanical ventilation days, 16% babies required more than 7 days of mechanical ventilation, 22% required 4-7 days and 62% required <3 days of mechanical ventilation. All babies with >7 days of mechanical ventilation had stage 2 or higher ROP, 63.6% of babies requiring 4-7 days had higher stages of ROP as compared to 38.7% of babies requiring less than 3 days of mechanical ventilation. Babies requiring longer duration of mechanical ventilation are at risk of higher incidence and severity of ROP compared to those with no or less requirement for mechanical ventilation. Babies based on duration of supplemental oxygen, 27% babies required 0-3 days of supplemental oxygen, 21% required for 4-7 days, 16% for 8-14 days, 8% required oxygen for 15-21 days and 28% required for >21 days. Incidence and severity of ROP was higher in those requiring prolonged duration of oxygen compared to those requiring less duration of oxygen. Babies with stage 2 or higher ROP was 96.4% in those with >21 days of oxygen requirement, 75% in 15-21 days group, 56.3% in those with 8-14 days, 33.3% in babies requiring 4-7 days of oxygen, 18.5% in those requiring oxygen for 0-3 days. Milder forms of stage 1 ROP was more in those with lower duration of oxygen requirement. Yang et al higher incidence with increased duration of ventilation.¹⁸ There are various studies determining the optimal saturation to be maintained for reducing morbidities and mortalities. 21% babies had BPD, requiring prolonged oxygen dependency. Incidence and severity of ROP was higher in this group compared to babies with no BPD. 95.5% of babies with BPD had stage 2 or higher ROP. This finding was similar to those in study by Holmstrom et al Significant association between retinopathy of prematurity and sepsis. 76% babies had sepsis.¹⁹ Stage II or higher of ROP was significantly higher in cases with sepsis (67.1%) compared to the cases with no sepsis (12.5%). Sepsis is an important risk factor for incidence and severity of ROP in preterm neonates. Study by Huang et al showed increased incidence of any form of ROP and severity with associated Sepsis.²⁰ Incidence of ROP was higher in babies having shock and requiring Inotropic support than those without shock. Stage II or higher of ROP was significantly higher in cases with shock (66.7%) compared to the cases with no shock (29.4%). This was similar to results from study by Wong, et al incidence of ROP in babies with Intraventricular hemorrhage shows higher incidence of ROP in those with any grade of IVH. 23% babies had IVH, 82.6% of these had stage 2 or higher level of ROP and 4.3% had milder stage I ROP.²¹ This shows significant association of IVH and development of ROP. Brown et al showed higher severity of ROP with IVH.²² Role of antenatal steroids

has been studied in various studies for its role in reduction of RDS, IVH, BPD. In this study 56% of mothers received complete or partial dose of steroids. Its correlation with reduction of RDS, IVH, BPD and further reduction in ROP need to be analysed in further studies.

CONCLUSION

These findings that anemia and number of blood transfusions are significant risk factors in the development of retinopathy of prematurity. Sepsis, Intraventricular hemorrhage, requirement for inotropes are also associated with incidence and progression of ROP. These are in addition to other predisposing factors low gestational age, low birth weight, longer duration of ventilation and oxygen requirement, BPD as a risk factor for ROP.

Recommendations

Minimizing blood investigations and associated blood loss as much as possible to reduce anemia and need for transfusion, proper antenatal screening and post-natal management of sepsis, minimizing duration of ventilation and supplemental oxygen just to maintain adequate saturation, regular screening of retinopathy of prematurity in preterm babies and adequate management of the same.

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