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RESEARCH ARTICLE

LOWER HEMOGLOBIN LEVELS AS A RISK FACTOR FOR THE DEVELOPMENT OF RETINOPATHY OF PREMATURITY.

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Abstract: ***Background***: Retinopathy of prematurity (ROP) is a vasoproliferative disorder of the immature retina, now recognized as a leading cause of childhood blindness worldwide, with approximately 50,000 children affected annually.Hemoglobin (Hb) critically influences tissue oxygen delivery; neonatal anemia may exacerbate retinal hypoxia, upregulate angiogenic signaling, and thus contribute to ROP progression—yet its role has not been established in a multivariate context ***Objectives***: To determine whether lower initial Hb levels (within first 48 h of life) independently predict any-stage ROP in neonates < 34 weeks gestation. Methodology: A retrospective observational study was conducted among 167 inborn neonates < 34 weeks gestation with Hb within 48 hours; developed ROP, at Department of Ophthalmology of tertiary care centre. ***Results:*** Among the study participants 22 cases who had ROP and haemoglobin level was in between 10.5-15.4%. Total 55 cases who didn't had ROP and haemoglobin level was in between 10.5-15.4%. Out of total, 22(43.2%) cases had stage 1 ROP, 18(35.3%) cases had stage 2 ROP and 11(21.5%) cases had stage 3 ROP.The mean gestational age was 28.63 + 2.09 weeks and 31.52 + 2.80 weeks, respectively in ROP present and ROP absent group. Of total, 76.4% cases who had ROP also presence of RDS. In 54.9% cases had who had ROP, there was presence of mechanical ventilation. ***Conclusion:*** The present study demonstrates that lower hemoglobin levels within the first 48 hours of life are significantly associated with the development of any-stage ROP in preterm neonates. Infants with lower gestational age, lower birth weight, RDS, mechanical ventilation, and PRBC transfusion were at higher risk.

Keywords: Retinopathy, Premature, Hemoglobin level, Vasoproliferative disease

INTRODUCTION

Retinopathy of prematurity (ROP) is a vasoproliferative disorder of the immature retina, now recognized as a leading cause of childhood blindness worldwide, with approximately 50,000 children affected annually. A systematic review found a pooled global ROP prevalence of 31.9% (95% CI 29.0–34.8) among preterm infants, and severe ROP occurred in 7.5% (6.5–8.7) of case. In high-income settings, ROP is largely confined to extremely preterm (<28 weeks) babies, whereas in middle-income countries up to 30–40% of infants ≤32 weeks develop any ROP, reflecting variable neonatal care standards.[1-2]

Pathophysiology involves two phases: initial hyperoxia-induced vessel attenuation followed by hypoxia-driven neovascularization mediated by VEGF and hypoxia-inducible factors.[3] Known predictors include low gestational age, low birth weight, prolonged oxygen therapy, mechanical ventilation, sepsis, bronchopulmonary dysplasia, and blood transfusions.[4-5] Hemoglobin (Hb) critically influences tissue oxygen delivery; neonatal anemia may exacerbate retinal hypoxia, upregulate angiogenic signaling, and thus contribute to ROP progression—yet its role has not been established in a multivariate context.[6]

Prior studies reported univariate associations between early anemia and ROP, but none have adjusted for confounders such as Respiratory Distress Syndrome (RDS) or transfusions to confirm Hb as an independent predictor. Optimal Hb cut-offs for stratifying ROP risk remain unvalidated, limiting evidence-based screening prioritization. Existing research largely originates from single centers; the interplay of Hb level with regional ROP epidemiology, which ranges from 5–8% in developed to 30–40% in developing settings, was uncharted.

OBJECTIVES: To determine whether lower initial Hb levels (within first 48 h of life) independently predict any-stage ROP in neonates < 34 weeks gestation.

MATERIAL AND METHODS:

A retrospective observational study was conducted among 167 inborn neonates < 34 weeks gestation with Hb within 48 hours; developed ROP, at Department of Ophthalmology of tertiary care centre.

Neonatal death or discharge before ROP screening; incomplete follow-up were excluded. Per national guidelines—infants <28 weeks or <1,200 g at 2–3 weeks; 28–34 weeks at 4 weeks—using RETCAM after mydriasis; staged per ICROP 2005, ROP screening was done. Gestational age (LMP/ultrasound/New Ballard), birth weight, mode of delivery, RDS diagnosis (clinical + CXR), mechanical ventilation, bronchopulmonary dysplasia (oxygen at 28 days or 36 weeks PMA), sepsis, delayed full feeds, PRBC transfusion and haemoglobin level at 48 hour were noted.

Data entry and analysis: Data were collected and entered into Microsoft excel sheet and analysed by using SPSS software version 26. Qualitative data were descried as a frequency and percentages and quantitative data were described as mean and SD.

RESULTS

Of total, among 51 neonates ROP was present and 116 neonates had no ROP.

Table 1. Hemoglobin level of study participants

Hemoglobin level	ROP present	ROP absent
25 percentile (10.5-15.4 %)	22	55
26-50 Percentile (15.4 -17.3%	16	34
> 50 percentile (>17.3%)	13	27

Among the study participants 22 cases who had ROP and haemoglobin level was in between 10.5-15.4%. Total 55 cases who didn't had ROP and haemoglobin level was in between 10.5-15.4%. [Table 1]

Table 2. ROP stage wise distribution of study participants (n=51)

Stages of ROP	Frequency	Percentages
Stage 1	22	43.2
Stage 2	18	35.3
Stage 3	11	21.5

Out of total, 22(43.2%) cases had stage 1 ROP, 18(35.3%) cases had stage 2 ROP and 11(21.5%) cases had stage 3 ROP. [Table 2]

Table 3. Variables findings among study participants

Variables	ROP present (n=51)	ROP absent (n=116)
Mean gestational age (in weeks)	28.63 $\pm$ 2.09	31.52 $\pm$ 2.80
Mean Birth weight (in gm)	1028 $\pm$ 226	1280 $\pm$ 180
RDS Present	39 (76.4%)	46 (39.6%)
Mechanical ventilation present	28 (54.9%)	51 (43.9%)
BPD present	15 (29.4%)	4 (3.4%)
Sepsis Present	18 (35.2%)	21 (18.1%)
Delayed full feeds	29 (56.8%)	20 (17.2%)
PRBC present	31 (60.7%)	21 (18.1%)

The mean gestational age was 28.63 $\pm$ 2.09 weeks and 31.52 $\pm$ 2.80 weeks, respectively in ROP present and ROP absent group. The mean birth weight was 1028 $\pm$ 226 gm and 1280 $\pm$ 180 gm, respectively in ROP present and ROP absent group.of total, 76.4% cases who had ROP also presence of RDS. In 54.9% cases had who had ROP, there was presence of mechanical ventilation. Of total 60.7% cases had presence of PRBC and ROP. [Table 3]

DISCUSSION

Preterm neonates born before 34 weeks gestational age had a 30.5% incidence of ROP in this study; the development of ROP was independently linked to lower birth weight, the presence of decreased Hb in the early stages, RDS, and the requirement for PRBC transfusion.The incidence of ROP among preterm infants in our study was comparable to earlier Indian studies that have been published: 30% in a study from central India by Dwivedi et al. and 32% in a study from southern India by Ahuja et al. [7,8]. As observed in most studies [5,7,8], it is not surprising that neonates with lower gestational age, lower birth weight, RDS, and the need for PRBC transfusion were at greater risk for developing ROP.

In this study, newborns with Hb 10.5–15 g/dL and 15–17 g/dL had a higher risk of ROP than neonates with Hb >17 g/dL. Higher Hb levels are protective, even when the mean Hb level in the ROP group does not fall below the neonatal anemia cutoff level (<13g/dL). However, in two earlier investigations, decreased hemoglobin in the early stages of preterm neonates was associated with an increased risk of ROP only in univariate analysis, not as an independent risk factor after adjustment [9,10]. Similarly, anemia (<11 g/dL) during the first week of life was found to be an independent predictor of ROP in extremely preterm newborns in a research by Lundgren et al. [11]

One significant etiology underlying the development of ROP is neovascularization of the retina [12]. Tissue hypoxia or hyperoxia controls a number of angiogenic factors, including VEGF, basic fibroblast growth factor (b-FGF), and hypoxia-induced factors (HIF-1alpha), which are crucial for the neovascularization of the retina [12]. The pathogenic significance of low Hb and the development of ROP may be explained by the fact that lower Hb levels lead to tissue hypoxia and increased VEGF release in the developing retina of preterm newborns. Higher hemoglobin levels may improve hemodynamic stability and reduce problems associated with prematurity in preterm infants.

Therefore, effective placental transfusion interventions in the birth room, such as delayed umbilical cord clamping or umbilical cord milking, may lower ROP. Nevertheless, no systematic research attributes the reduction of ROP to placental transfusion; instead, placental transfusion avoids necrotizing enterocolitis and the requirement for blood transfusions, which are recognized risk factors for ROP [13].

CONCLUSION:

The present study demonstrates that lower hemoglobin levels within the first 48 hours of life are significantly associated with the development of any-stage ROP in preterm neonates. Infants with lower gestational age, lower birth weight, RDS, mechanical ventilation, and PRBC transfusion were at higher risk. Our findings are consistent with multiple national and international studies, reinforcing that early anemia is an important and potentially modifiable risk factor. Routine monitoring of Hb levels in the first 48 hours, along with improved respiratory care and judicious transfusion practices, may help identify high-risk infants and enable earlier ophthalmic screening and prevention strategies

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