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Original Research Article

A Study on Clinical Profile of Aggressive Posterior Retinopathy of Prematurity (APROP)

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Abstract

Background: Retinopathy of prematurity(ROP)is a vasoproliferative retinopathy that affects developing retinal blood vessels in very low birth weight premature infants (<1500 grams). Premature retina exposed to high concentration of oxygen, followed by abrupt withdrawal, easily undergoes uncontrolled vasculo-fibrotic proliferation and eventually results in retinal detachment. APROP is the most aggressive form of rapidly developing ROP and can cause severe visual impairments in newborns.

Aim: To study the clinical profile of APROP.

Materials & Methods: This retrospective case-control study was done in the Department of Ophthalmology of a tertiary care hospital of Southern Odisha since 1st April 2020 to 30th April 2022. Neonates born at or before 32 weeks of gestation and/or <1500 grams birth weight admitted in neonatal intensive care unit were included in the study along with neonates born after 32 weeks gestation or birth weights between 1.5 kg & 2 kg if they had any unstable neonatal course. 42 babies developing APROP were compared with 42 controls (with ROP not more than zone 2 stage 2) who were matched for gestational age and birth weight and they were evaluated for other risk factors.

Results: The mean age among cases was 24.3 whereas that of controls was 24.9. The mean birth weight among cases was 1762 grams whereas that of controls was 1820 grams. The mean gestational age among cases was 31.2 weeks whereas that of controls was 31.4 weeks. 22 (52.38%) of the cases had sepsis (CRP ≥10mg/L) as compared to 8 (19.04%) of the controls with p value < 0.001. 26 (61.90%) of the cases had oxygen exposure ≥5 days as compared to 11 (26.19%) of the controls and with p value < 0.001. 9 (21.43%) of the cases had thrombocytopenia (Platetlet count < 100000/µl) as compared to 2 (4.76%) of the controls with p value = 0.024.

Conclusion: Our study thus showed sepsis, oxygen exposure ≥5 days, thrombocytopenia and blood transfusion as significant risk factors for APROP.

Keywords: Retinopathy of Prematurity, APROP, sepsis, thrombocytopenia, blood transfusion, hyperbilirubinemia.

Introduction

Retinopathy of prematurity(ROP)is a vasoproliferative retinopathy that affects developing retinal blood vessels in very low birth weight premature infants (<1500 grams) [1]. Premature retina exposed to high concentration of oxygen, followed by abrupt withdrawal, easily undergoes uncontrolled vasculo-fibrotic proliferation and eventually results in retinal detachment [2]. It begins to develop between 32 to 34 weeks after conception, regardless of gestational age at delivery and has two distinct phases[3]. During the first acute phase, the normal vasculogenesis of the retina is disturbed by the relative hyperoxia of the extrauterine environment. This causes vaso-obliteration and non-vascularisation of some areas of anterior retina [4].

The subsequent hypoxia causes a second chronic phase, characterised by the proliferation of vascular and glial cells, arteriovenous shunt formation, occasionally leading to involution or permanent cicatricial changes and visual impairment [5,6]. The key pathological change is local ischemia with subsequent peripheral retinal neovascularisation. This may regress completely or leave sequelae like myopia, strabismus, anisometropia, amblyopia, glaucoma and cataract [7]. In its more severe forms, it results in severe visual impairment or blindness, both of which carry a high financial cost for the community but also a high individual cost by affecting the normal motor, language, conceptual and social development of the child.

AROP is the most aggressive form of rapidly developing ROP and can cause severe visual impairments in newborns. Till date there have been very few studies to find out the risk factors of AROP. Hence this study was done.

Materials and Methods

This retrospective case-control study was done in the Department of Ophthalmology of a tertiary care hospital of Southern Odisha since 1st April 2020 to 30th April 2022.Neonates born at or before 32 weeks of gestation and/or <1500 grams birth weight admitted in neonatal intensive care unit were included in the study along with neonates born after 32 weeks gestation or birth weights between 1.5 kg & 2 kg if they had any unstable neonatal course with risk factors like ventilation, oxygen requirement, use of surfactant, septicaemia, hyperbilirubinemia, intraventricular hemorrhage, patent ductusarteriosus, exchange transfusion, apnea and use of blood products.

Neonates > 32 weeks of gestation with a stable neonatal course, children with major congenital malformation, chromosomal aberration and any fatal disease were excluded from the study. Infants who were having unilateral or bilateral retinal or choroidal disease (excluding retinopathy of prematurity) ormedia opacity obstructing the fundal view or those infants who were highly dependent on oxygen and could not be removed from the incubator for examination were also excluded from study. A retrospective 1:1 case control study was carried out in our college from 01/04/2020 to 30/04/2022 in which 42 babies developing APROP were compared with 42 controls (with ROP not more than zone 2 stage 2) who were matched for gestational age and birth weight and they were evaluated for other risk factors.

Statistical Analysis

Numerical data like birth weight, gestational age at birth etc were presented as mean scores and Student's T test was used to compare the means between two groups (case and control). Entire data was calculated on 95% CI. A p value <0.05 was considered significant.

Results

The possible confounding factors like age, birth weight and gestational age were matched effectively in both the groups. The mean age among cases was 24.3 whereas that of controls was 24.9 which was statistically insignificant (p value 0.778). The mean birth weight among cases was 1762 grams whereas that of controls was 1820 grams which was statistically insignificant (p value 0.116). The mean gestational age among cases was 31.2 weeks whereas that of controls was 31.4 weeks which was statistically insignificant (p value 0.552).

Table 1: Matching of cases and controls

Parameters	Cases (Mean)	Control (Mean)	P value
Age	24.3	24.9	0.778
Birth Weight	1762	1820	0.116
Gestational Age	31.2	31.4	0.552

22 (52.38%) of the cases had sepsis(CRP ≥10mg/L) as compared to 8 (19.04%) of the controls with p value < 0.001, suggesting that sepsis was a highly significant risk factor. 26 (61.90%) of the cases had oxygen exposure ≥5 days as compared to 11 (26.19%) of the controls and with p value < 0.001, suggesting that duration of oxygen exposure was a highly significant risk factor. 9 (21.43%) of the cases had thrombocytopenia (Platetlet count< 100000/µl)as compared to 2 (4.76%) of the controls with p value = 0.024, suggesting it was significant. 11 (26.19%) of the cases had blood transfusions as compared to 3 (7.14%) of the controls with (p value = 0.019), suggesting it was significant.

7 (16.67%) of the cases were of multiple gestation as compared to 5 (11.9%) of the controls with (p value = 0.553), suggesting it was insignificant. 13 (30.95%) of the cases were found to have hyperbilirubinemia as compared to 10 (23.8%) of the controls with (p value = 0.463), suggesting it was insignificant. 6 (14.28%) of the cases were found to be hyperglycemic as compared to 5 (11.9%) of the controls with (p value = 0.746), suggesting it was insignificant.

Table 2: Comparison between cases and controls

Risk factors	Cases	Control	P value
Sepsis	22	8	<0.001
Oxygen exposure	26	11	<0.001
Thrombocytopenia	9	2	0.024
Blood transfusion	11	3	0.019
Multiple gestation	7	5	0.553
Hyperbilirubinemia	13	10	0.463
Hyperglycemia	6	4	0.746

Figure 1 & 2: shows APROP and figure 3 shows a control patient.

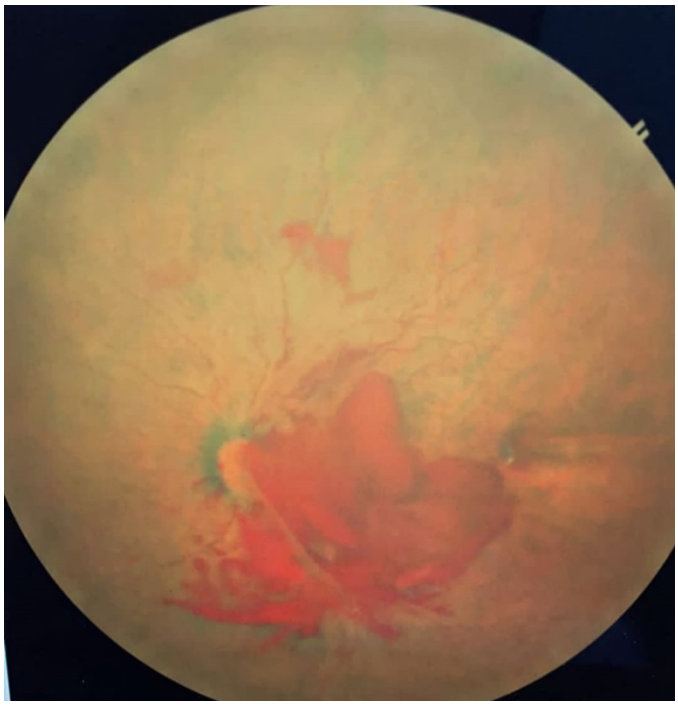

Figure 1: A patient with APROP& retinal hemorrhage.

Figure 2: Patient with APROP

Figure 3: A control patient

Discussion

The possible confounding factors like age, birth weight and gestational age were matched effectively in both the groups. 22 of the cases had sepsis as compared to 8 in controls and it was highly significant. This is comparable to the study by Lundgren *et al* which also showed sepsis as a significant factor [8]. Lundgren *et al* in their study also found, all APROP cases postnatally developed at least two infectious episodes, one in the first month and one around the time of ROP diagnosis.

All APROP cases exhibited thrombocytopenia in the first month, and 6/9 exhibited thrombocytopenia around the time of ROP diagnosis. Compared to the controls, APROP cases more frequently developed necrotizing enterocolitis (8/9 vs. 1/9; $p < 0.01$) and sepsis (9/9 vs. 3/9; $p < 0.01$), and they had significantly lower median platelet counts (90 × 109/l, range 4-459, vs. 158 × 109/l, range 20-500; $p < 0.001$) [8]. In our study 9 of the cases had thrombocytopenia as compared to 2 of the controls and it was significant. In our study 26 of the cases had oxygen exposure ≥5 days as compared to 11 of the controls and it was highly significant. The study by Sanghi *et al* is also comparable to our study showing oxygen exposure as a significant factor [9]. 11 of the cases had blood transfusions as compared to 3 of the controls and it was also found to be significant. There was no significant difference in multiple gestation, hyperbilirubinemia, and neonatal hyperglycemia when cases were compared with controls.

In our study, the mean birth weight among cases was 1762 grams whereas that of controls was 1820 grams and mean gestational age was 31.2 weeks in cases. Jalali *et al* in their study found, the mean birth weight and gestational age were 1791.27 ± 281.86 g (range, 1500-2300 g) and 30.7 ± 1.03 weeks (range, 29-32 weeks), respectively[9]. It's almost similar to our study. Sen *et al* in their study found mean gestational age was 29.1 weeks, and mean birth weight was 1226.9 gms[10]. In their study they also found Sixty-six (75.8%) eyes had Type I ROP and 21 (24.1%) eyes had APROP at presentation. Of 82 eyes, 80.5% (66 eyes) showed regression of ROP following combination treatment and 19.5% (16 eyes)

needed surgery. Of these, 15 underwent surgery and 12 had successful outcome. 95.1% (78 eyes) had attached retina at posterior pole and 4.9% (4 eyes) had detached retina[10]. In our study, 26 (61.90%) of the cases had oxygen exposure ≥5 days. In the study by Jalali *et al*, the oxygen exposure was 7-23 days. They also found 24.1% eyes had an unfavourable outcome [9].

Conclusion

Our study thus showed sepsis, oxygen exposure ≥5 days, thrombocytopenia and blood transfusion as significant risk factors. Multiple gestation, hyperbilirubinemia, and neonatal hyperglycemia were found to be insignificant in our study. All babies with above risk factors should be screened regularly and babies diagnosed with APROP need urgent treatment and rigorous follow up.

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