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# Neonatal risk Factors and their Correlation with Severity and Stages of Retinopathy of Prematurity: A Five-Year Retrospective Study in a District General Hospital

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## Abstract

***Introduction:*** *Retinopathy of prematurity is a largely preventable condition with appropriate screening and early intervention. A comprehensive study of risk factors and knowledge on the pathophysiology is of great importance to help clinicians predict high-risk patients. This paper aims to further identify risk factors of ROP and correlate them with different stages (severity) of ROP.*

***Methods:*** *A retrospective review of all preterm infants admitted to neonatal intensive care unit (NICU) in ELHT from January 2015 to December 2019. All infants screened and included were based on the screening criteria set out by the Royal College of Ophthalmologists.*

***Results:*** *Among 415 infants included, 199(48.0%) were male with gestational age of 28.90±2.72 weeks and mean birth weight of 1214.42±350.81g. The incidence of bilateral intraventricular haemorrhage (IVH) is higher in infants with stage 3 ROP (34.8%, P=0.002). Neonates who were Asian in ethnicity were more likely to have stage 3 ROP requiring laser treatment (60.9%, P=0.008; 66.7%, P=0.040). Units of blood transfusion and duration of ventilation were highly associated with severe ROP (5.26 ± 3.22, P<0.001; 31.13 ± 24.59, P<0.001) and ROP that required treatment (6.89 ± 6.17, P<0.001; 41.56 ± 37.02, P<0.001). Logistic regression analysis also revealed significant association between Asian ethnicity (OR: 0.289, CI:0.101-0.823), bilateral IVH (OR:1.895, CI:1.035-3.471), unit of blood transfusion (OR: 1.205, CI:1.028-1.413) with severe ROP and ROP requiring treatment.*

*Conclusion: Bilateral IVH, units of blood transfusion, bronchopulmonary dysplasia, and Asian ethnicity are associated with severe ROP and ROP requiring treatment.*

## Introduction

Retinopathy of prematurity (ROP) is a largely preventable condition limited to the developing retinal vasculature of preterm infants, especially those weighing less than 1251g. There are six stages of severity, where stages one and two are considered 'mild' and often resolve spontaneously without any intervention. Stages three, four, five and any ROP with plus disease (venous dilatation and arterial tortuosity at the posterior pole, pupil rigidity, iris vascular engorgement and vitreous haze) are considered 'severe' and pose a risk for poor visual outcome [1,2]. ROP was first described in 1941 as 'Retrolental Fibroplasia' and was first reported to be associated with prematurity in 1942 by Dr Theodore L. Terry, hence the name 'Terry Syndrome' [2,3]. By the 1950s, oxygen was found to be an important link to the pathogenesis of this potentially sight threatening condition thus its use among premature infants was immediately restricted. [3,4]. Recent studies have established that several other risk factors other than oxygen contribute directly or indirectly to the pathogenesis of ROP, like birth weight (BW), gestational age (GA), prolonged mechanical ventilation, Apgar score, bronchopulmonary dysplasia (BPD), anaemia, sepsis and intraventricular haemorrhage (IVH) [2,5]. The prevalence of ROP is higher in resource poor settings and developing countries where there is a lack of awareness of risk factors and their progression, limited resources in monitoring blood oxygenation and the scarcity of skilled professionals [6]. It is estimated that almost 10% of all births Worldwide are premature (<37 weeks gestation) [5]. In the United Kingdom alone, ROP was responsible for around 5-8% of childhood blindness (both partial and complete) in years 1985-1990, reducing to 3% in year 2000 after guidelines for ROP screening emerged in 1990 [1,7]. With advancements in neonatal care, survival rates of premature infants, especially those at the extremes of gestational age and borderline viability (22-24 weeks), have improved thereby increasing the incidence of ROP and the subsequent increase in the number of infants needing screening [1,8]. A comprehensive study of risk factors and knowledge on the pathophysiology is of great importance to help clinicians predict high-risk patients and to prevent the progression of ROP to severe stages. This study aims to further identify risk factors of ROP and correlate them with different stages (severity) of ROP.

## Materials and Methods

This was a retrospective review of all preterm infants admitted to neonatal intensive care unit (NICU) in East Lancashire Teaching Hospital NHS Trust from January 2015 to December 2019. All infants screened and included were based on the screening criteria set out by the Royal College of Ophthalmologists and the Royal College of Paediatrics and Child Health.

### Screening Criteria and Protocol

- All infants born at GA <32 weeks or BW <1501g.
- All infants born <27 weeks were screened at 30-31 weeks postmenstrual age.
- All infants born between 27–32 weeks were screened at 4–5 weeks of postnatal age.
- All infants born >32 weeks but BW <1501g were screened at 4-5 weeks of postnatal age.
- All infants were screened before being discharged from the hospital.

Infants who did not meet the criteria for screening and infants who were seen and followed up for other reasons i.e. congenital glaucoma were excluded from the study.

Retinal screening and examination of all infants was performed in NICU using a binocular indirect ophthalmoscope (Heine Sigma 250 Binocular Indirect) and a 28-dioptre Volk lens. Paediatric speculum and a paediatric scleral depressor were used when necessary for the examination of retinal periphery. Screening was carried out by a single clinician. Retinal examination was performed under mydriasis with one drop of phenylephrine 2.5% and cyclopentolate 0.5%, instilled in two doses, each 15 minutes apart, an hour before examination. All infants were graded based on the International Classification of Retinopathy of Prematurity (ICROP) [1,5,9]. Infants requiring treatment based on the results of the Early Treatment of Retinopathy of Prematurity Study and Royal College guidelines were referred to tertiary care centres accordingly [1,10].

Data including; gender, race, type of birth (multiple versus singleton), gestational age (GA), birth weight (BW), mode of delivery, initial stage of ROP, highest stage of ROP recorded, evidence of IVH (laterality = unilateral versus bilateral; and grade), evidence of jaundice, number of blood transfusions, details of respiratory support – (number of days on mechanical ventilation, continuous positive airway pressure (CPAP) and high flow nasal cannula (HFNC)) and Apgar scores at 1, 5 and 10 minutes were gathered from the unified NHS BadgerNet system - an electronic patient recording system that records real-time events within a neonatal unit on a daily basis. All data was compared to handwritten documentation for each patient in the ROP folders in NICU to reduce the occurrence of missing data, due to the retrospective nature of the study.

Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS) software version 25.0. Descriptive data was presented as mean ± standard deviation (SD) (range) whilst quantitative data were expressed as a percentage. In order to predict the significant independent variable, Chi-squared test was used to compare all the categorical variables. One-way ANOVA with post-hoc Bonferroni adjustment was used to compare the continuous variables between three different sample groups. The level of significance was set at 2-tailed P <0.05.

The association between severe ROP and significant independent variable on univariate analysis was assessed with binary logistic regression.

### Patient involvement

Patients were not directly involved in the design of this study.

## Results

Of the 415 patients included in this study, 199 (48.0%) were male and 216 (52.0%) were female with the mean GA of 28.90 ± 2.72 weeks and mean BW of 1214.42 ± 350.81. 259 (62.4%) of them were Caucasians, 155(37.3%) were Asians and one (0.2%) was Afro-Caribbean. 77 infants were twins and the rest were singletons. Upon screening, 347 infants (83.6%) with GA of 29.48 ± 2.46 weeks (18-35) did not develop ROP, 68 (16.4%) had ROP. The latter group included 12 infants (17.6%) with stage 1 ROP (mean GA of 26.50 ± 1.93 (24-29)), 33 (48.5%) with stage 2 ROP (mean GA of 26.36 ± 1.20 (23-30)) and 23 (33.8%) with stage 3 ROP (mean GA of 25.09 ± 1.56 (23-29)). None of the patients developed stage 4 and 5 ROP. Among the 68 infants who developed ROP, 9 (12.7%) of them required laser therapy. The difference in GA was statistically different (P<0.001) when compared to infants with no ROP.

Our study had mean GA of 28.90 ± 2.72 (18-35). We divided the GA into the following groups:

- GA <27 weeks,
- 27-32 weeks and
- > 32 weeks.

GA were <27 weeks in 92 (22.2%) cases, between 27-32 weeks in 269 (64.8%) cases and >32 weeks in 54 (13.0%) cases. Of all patients with BW <1501g, 268 (77.2%) had no ROP, 12 (3.6%) had stage 1 ROP, 33 (8.0%) had stage 2 ROP and 23 (5.5%) had stage 3 ROP.

We combined the GA and BW and divided these patients into five groups of GA and BW.

- Group 1: GA <27 weeks and BW <1501g (91 cases [21.9%] of which 46 had no ROP, 7 developed stage 1 ROP, 20 developed stage 2 ROP and 18 developed stage 3 ROP).
- Group 2: GA 27-32 weeks and BW <1501g (194 cases [46.7%] of which 172 had no ROP, 5 had stage 1 ROP, 12 had stage 2 ROP and 5 had stage 3 ROP).
- Group 3: GA ≥ 32 weeks and <1501g (52 cases [12.5%] of which all 52 had no ROP).
- Group 4: GA <32 weeks and ≥1501g (78 cases [18.8%] of which 77 had no ROP and 1 with stage 2 ROP).

We further analysed our data and noted that none of these cases ≥30 weeks gestation had ROP and that 7 of our cases ≥1251g had ROP, 2 of which progressed to stage 1 ROP and 5 cases progressed to stage 2 ROP. (Table 1) reveals the clinical characteristics of these 7 patients ≥1251g who developed ROP. Interestingly, none of these infants had jaundice, blood transfusion or IVH and one baby had a birth weight >1501g.

(Table 2) shows the results of univariate analysis comparing cases with no ROP and stages 1,2 and 3 ROP. We noted statistically significant differences in all variables except from gender and type of birth (singleton versus twin pregnancy. With regard to ethnicity, we note that approximately two-thirds of infants with stage 1 ROP were Caucasians and one-third were Asians. This is inverse for stages 2 and 3 ROP where approximately two-thirds were Asians and one-third were Caucasian (P=0.008). IVH is more commonly seen in stage 3 ROP as compared to other groups. (P=0.001). In terms of laterality of IVH, premature infants with no ROP are more likely to have unilateral IVH but infants with ROP at all stages are more likely to have bilateral IVH. (P=0.001) Further detailed results on IVH showed that bilateral IVH was significantly associated with ROP stage 3 as compared to other groups.

With regards to risk factors associated with unit of blood transfusion, the mean number of transfusion unit in stage 3 ROP is 5.26±3.22 (0-11), the highest across the group (P<0.001) and similar findings are seen in (Table 3), indicating significant relationship between unit of blood transfusion and severe ROP. A similar trend is witnessed in ventilation variable, in that infants with higher stages of ROP and ROP requiring treatment (Table 3) received longer duration of ventilation (P<0.001). Another significant risk factor was Patent Ductus Arteriosus (PDA), 15 (65.2%) of in ROP Stage 3 (P<0.001) had PDA and 6 (66.7%) required laser treatment (P<0.001). The incidence of bronchopulmonary dysplasia (BPD) was significantly higher in infants with Stage 3 ROP (P<0.001) and ROP requiring treatment (P<0.001).

The binary logistic regression in severe ROP model (Table 4) (R2=0.440 for model 1, R2=0.411) shows that Asian ethnicity (P=0.020, OR:0.289, CI:0.101-0.823), bilateral IVH (P=0.038, OR:1.895, CI:1.035-3.471), GA (P=0.002, OR:0.678, CI:0.530-0.868) and duration of ventilation (P=0.028, OR:1.045, CI:1.005-1.086) has significant effect in predicting risk factor of severe ROP in the first model. When comparing the incident of severe ROP in different combination of independent variables, it was noted

**Table 1.** *Detailed Profile Of 7 ROP Infants With BW ≥ 1250g.*

| No | Gestational Age (weeks) | Weight (g) | Gender | Race | ROP Stage | Delivery | Jaundice | Transfusion | Treatment | CPAP, days | Ventilation, days | HFNC, days | IVH | PDA |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 29+3 | 1435 | F | Caucasian | 1 | Emergency C SEC | No | No | No | 0 | 1 | 14 | No | No |
| 2 | 26+6 | 1485 | M | Caucasian | 1 | Elective C SEC | No | No | No | 0 | 2 | 4 | No | No |
| 3 | 29+5 | 1277 | M | Caucasian | 2 | Elective C SEC | No | No | No | 0 | 13 | 0 | No | Yes |
| 4 | 29+5 | 1277 | F | Asian | 2 | Elective C SEC | No | No | No | 0 | 13 | 0 | No | No |
| 5 | 29+0 | 1330 | F | Caucasian | 2 | SVD | No | No | No | 0 | 1 | 0 | No | No |
| 6 | 28+3 | 1550 | M | Caucasian | 2 | Emergency C SEC | No | No | No | Yes (11) | 10 | 30 | No | Yes |
| 7 | 29+6 | 1360 | M | Caucasian | 2 | SVD | No | No | No | Yes (2) | 0 | 0 | No | No |

*CPAP: Continuous Positive Airway Pressure, HFNC HFNC: High Flow Nasal Cannula , IVH: Intraventricular Haemorrhage, PDA: Patent Ductus Arteriosus

that without ventilation, blood transfusion and BPD were found to be significantly associated with severe ROP in Model 2 and 3 respectively.

## Discussion

In order to identify premature infants at risk of developing ROP, screening criteria including BW and GA have been set high to ensure that all infants requiring treatment are assessed. The current ROP guideline in the United Kingdom recommends that all infants with GA <31 weeks and BW <1251g must be screened and all infants with GA <32 weeks and BW <1501g should be screened [1]. Studies have shown that the reduction of screening criteria to <30 weeks GA and <1251g BW would have led to some missed diagnosis of ROP with the data available back in the 1980s. Data from personal practice among the guideline group has also confirmed sight threatening ROP in eight infants with BW >1250 and GA >30 between years 2000-2008 [1,11]. Despite the low specificity of screening (17% screened has ROP in our study), we have not missed any infants with ROP during this study period (100% sensitivity). Using our study data, reducing the screening criteria from BW<1501g to <1251g and GA from <32 to <30 weeks would not lead to any missed ROP, as shown in (Table 1). We compare our screening criteria to other countries. Countries such as the USA (≤ 30 weeks or ≤ 1500g), Canada (≤30 weeks or ≤1250g), Australia (<30 weeks or <1250g) the Netherlands (<30 weeks or <1250g) screen fewer infants compared to the United Kingdom [12]. Nonetheless we do have to take into consideration the heterogeneity between populations of different countries. Some may argue that we may be over-screening infants for ROP leading to unnecessary distress to both infants and parents. Furthermore, with the increasing number of premature infants due to advancing neonatal care, low specificity screening could impose a huge burden on the healthcare system. To improve the specificity and sensitivity of ROP screening, Binenbaum and colleagues have incorporated and validated the Postnatal Growth and Retinopathy of Prematurity screening criteria (G-ROP) in North America and Canada, which comprise of BW, GA and weight gain prediction model. This has shown to reduce the number of infants requiring screening by 35.6% [13]. However, this should only be applicable to countries with advanced neonatal care with strict oxygen monitoring.

The GA of all infants in our study (29.0 ± 2.8 weeks) is quite similar to a study published by Goble and colleagues in a cohort of 1427 infants in Birmingham between 1985-1995, where their mean GA was 29.1 ± 2.1 weeks. Amongst infants with stage 3 ROP, our mean GA was 25.1 ± 1.6 weeks compared to theirs at 26.5 ± weeks [14]. In addition to what has already been mentioned, we are now screening smaller infants due to the advancing neonatal care.

Blood transfusion is strongly associated with the development of ROP. Our results indicate that the incidence of severe ROP is associated with higher unit of blood transfusion [5,15-17]. A prospective cohort study between 2012-2013 found that preterm infants who developed ROP had significantly lower foetal haemoglobin (HbF) as compared to those who did not develop ROP [18]. Infants with lower HbF are more likely to be unwell and require more blood transfusion. Lower HbF and higher adult haemoglobin (HbA) as a result of blood transfusion provides higher oxygen delivery to the developing retina, as HbA has lower affinity to oxygen [18,19]. Furthermore, with the low iron-binding capacity of preterm infants and deficiency in free iron protection due to low transferrin, large amounts of free iron from packed red blood cells would speed up fenton reaction with subsequent formation of highly reactive oxygen free radicals, which contributes to the development of ROP [16,19,20].

***Table 2.*** *Clinical Characteristics Of Patients Without ROP And With ROP at Different Stages.*

| | All Patient | No ROP | ROP Stage 1 | ROP Stage 2 | ROP Stage 3 | P Value |
|---|---|---|---|---|---|---|
| Clinical Characteristics | n=415 | n=347 | n=12 | n=33 | n=23 | |
| Gestation Age, mean ± SD (Range), weeks | 28.90 ± 2.72 (18-35) | 29.48 ± 2.46 (18-35) | 26.50 ± 1.93 (24-29) | 26.36 ± 1.20 (23-30) | 25.09 ± 1.56 (23-29) | <0.001b |
| Gestation Age Category, n (%): | | | | | | <0.001a |
| <27 WEEKS | 92 (22.2) | 46 (13.3) | 7 (58.3) | 20 (60.6) | 19 (82.6) | |
| 27-32 WEEKS | 269 (64.8) | 247 (71.2) | 5 (41.7) | 13 (39.4) | 4 (17.4) | |
| >32 WEEKS | 54 (13.0) | 54 (15.6) | 0 | 0 | 0 | |
| Birth Weight, mean ± SD (Range), g | 1214.42 ± 350.81 (430-2451) | 1280.78 ± 327.94 (500-2451) | 1062.92 ± 256.34 (710-1485) | 900.58 ± 267.09 (480-1550) | 742.52 ± 159.51 (685-1115) | <0.001b |
| Less Than 1.5 kg, n (%) | 335 (80.7) | 268 (77.2) | 12 (100) | 32 (97) | 23 (100) | 0.001a |
| Gender, n (%) | | | | | | 0.936a |
| Male | 199 (48) | 164 (47.3) | 6 (50) | 17 (51.5) | 12 (52.2) | |
| Female | 216 (52) | 183 (52.7) | 6 (50) | 16 (48.5) | 11 (47.8) | |
| Twins, n (%) | 77 (18.6) | 62 (17.9) | 5 (41.7) | 6 (18.2) | 4 (17.4) | 0.224a |
| Twins Mean Gestation age, mean ± SD (Range), weeks | 28.56 ± 2.72 (18-34) | 29.16 ± 2.58 (18-34) | 26.60 ± 0.89 (26-28) | 25.50 ± 1.87 (23-28) | 26.25 ± 2.50 (23-29) | 0.001b |
| Race, n (%): | | | | | | 0.008a |
| Asian | 155 (37.3) | 125 (36.0) | 4 (33.3) | 12 (36.4) | 14 (60.9) | |
| White | 259 (62.4) | 222 (64.0) | 8 (66.7) | 20 (60.6) | 9 (39.1) | |
| Afro-Caribbean | 1 (0.2) | 0 | 0 | 1 (3.0) | 0 | |

| | All Patient | No ROP | ROP Stage 1 | ROP Stage 2 | ROP Stage 3 | P Value |
|---|---|---|---|---|---|---|
| Weeks And Weight, n (%): | | | | | | <0.001a |
| <27 weeks AND < 1501g | 91 (21.9) | 46 (13.3) | 7 (58.3) | 20 (60.6) | 18 (78.3) | |
| 27-32 weeks AND < 1501g | 194 (46.7) | 172 (49.6) | 5 (41.7) | 12 (36.4) | 5 (21.7) | |
| >32 weeks AND < 1501g | 52 (12.5) | 52 (15.0) | 0 | 0 | 0 | |
| <32 weeks AND ≥ 1501g | 78 (18.8) | 77 (22.2) | 0 | 1 (3.0) | 0 | |
| > 1250g, n (%) | 209 (50.4) | 202 (58.2) | 2 (16.7) | 5 (15.2) | 0 | <0.001a |
| Delayed In Screening, n (%) | 28 (6.7) | 20 (5.8) | 0 | 4 (12.1) | 4 (17.4) | 0.070a |
| Treatment, n (%) | 9 (2.2) | 0 | 0 | 1 (3.0) | 8 (34.8) | <0.001a |
| Jaundice, n (%) | 163 (39.4) | 126 (26.4) | 5 (41.7) | 19 (57.6) | 13 (56.5) | 0.033a |
| BPD, n (%) | 85 (20.5) | 54 (15.6) | 6 (50) | 12 (36.4) | 13 (56.5) | <0.001a |
| IVH, n (%) | 84 (20.2) | 62 (17.9) | 2 (16.7) | 8 (24.2) | 12 (52.2) | 0.001a |
| Head Scan Results, n (%): | | | | | | 0.002a |
| Normal | 331 (79.8) | 285 (82.1) | 10 (83.3) | 25 (75.8) | 11 (47.8) | |
| Unilateral IVH | 42 (10.1) | 34 (9.8) | 1 (8.3) | 3 (9.1) | 4 (10.8) | |
| Bilateral IVH | 42 (10.1) | 28 (8.1) | 1 (8.3) | 5 (15.2) | 8 (34.8) | |
| Transfusion Unit, mean ± SD (Range) | 1.17 ± 2.46 (0-21) | 0.67 ± 1.64 (0-10) | 2.25 ± 3.84 (0-11) | 3.28 ± 4.18 (0-21) | 5.26 ± 3.22 (0-11) | <0.001b |
| Ventilation Days, mean ± SD (Range) | 6.92 ± 12.91 (0-101) | 4.02 ± 7.12 (0-53) | 8.83 ± 11.91 (0-38) | 19.45 ± 21.29 (0-101) | 31.13 ± 24.59 (2-90) | <0.001b |
| PDA, n (%) | 36 (8.7) | 9 (2.6) | 2 (16.7) | 10 (30.3) | 15 (65.2) | <0.001a |

a Chi Square Test was used for analysis of categorical variables
b One-Way ANOVA was used for analysis of continuous variables

***Table 3:*** *Clinical Characteristics Of Patients With ROP Requiring Treatment And Not Requiring Treatment.*

| | All cases | No ROP | ROP Requiring Treatment | ROP Not Requiring Treatment | P Value |
|---|---|---|---|---|---|
| | n=415 | n=347 | n= 9 | n=59 | |
| Clinical Characteristics | | | | | |
| Gestation Age (weeks), mean ± SD (Range) | 28.90 ± 2.72 (18-35) | 29.48 ± 2.46 (18-35) | 24.33 ± 1.23 (23-26) | 26.2 ± 1.90 (23-30) | <0.001b |
| Gestation Age Category, n (%): | | | | | <0.001a |
| <27 WEEKS | 92 (22.2) | 46 (13.3) | 9 (100) | 37 (62.7) | |
| 27-32 WEEKS | 268 (64.6) | 247 (71.2) | 0 | 22 (37.3) | |
| >32 WEEKS | 53 (12.8) | 54 (15.6) | 0 | 0 | |
| Birth Weight (g), mean ± SD (Range) | 1214.42 ± 350.81 (430-2451) | 1280.78 ± 327.94 (500-2451) | 721.44 ± 112.09 (550-875) | 899.31 ± 264.80 (430-1550) | <0.001b |
| Less Than 1500g, n (%) | 335 (80.7) | 268 (77.2) | 9 (100) | 58 (98.3) | 0.001a |
| Gender, n (%) | | | | | 0.789a |
| Male | 199 (48) | 164 (47.3) | 5 (55.6) | 29 (49.2) | |
| Female | 216 (52) | 183 (52.7) | 4 (44.4) | 30 (50.8) | |
| Twins, n (%) | 77 (18.6) | 62 (17.9) | 2 (22.2) | 13 (22.0) | 0.719a |
| Twins Mean Gestation age, mean ± SD (Range) | 28.56 ± 2.72 (18-34) | 29.16 ± 2.58 (18-34) | 23 ± 0 (23-23) | 26.54 ± 0.37 (24-29) | <0.001b |
| Race, n (%): | | | | | 0.040a |
| Asian | 155 (37.3) | 125 (36.0) | 6 (66.7) | 24 (40.7) | |
| White | 259 (62.4) | 222 (64.0) | 3 (33.3) | 34 (57.6) | |
| Afro-Caribbean | 1 (0.2) | 0 | 0 | 1 (1.7) | |
| Weeks And Weight, n (%): | | | | | <0.001a |
| <27 weeks AND < 1501g | 91 (21.9) | 46 (13.3) | 8 (88.9) | 37 (62.7) | |
| 27-32 weeks AND < 1501g | 194 (46.7) | 172 (49.6) | 1 (11.1) | 21 (35.6) | |
| >32 weeks AND < 1501g | 52 (12.5) | 52 (15.0) | 0 | 0 | |
| <32 weeks AND ≥ 1501g | 78 (18.8) | 77 (22.2) | 0 | 1 (1.7) | |
| > 1250g, n (%) | 209 (50.4) | 202 (58.2) | 0 | 7 (11.9) | <0.001b |
| Delayed In Screening, n (%) | 28 (6.7) | 0 | 2 (22.2) | 6 (10.2) | 0.080a |
| Jaundice, n (%) | 163 (39.4) | 126 (26.4) | 5 (55.6) | 32 (54.2) | 0.021a |
| BPD, n (%) | 85 (20.5) | 54 (15.6) | 6 (66.7) | 25 (42.4) | <0.001a |
| IVH, n (%) | 84 (20.2) | 62 (17.9) | 4 (44.4) | 18 (30.5) | 0.016a |
| Head Scan Results, n (%): | | | | | 0.003a |
| Normal | 331 (79.8) | 285 (82.1) | 5 (55.6) | 41 (69.5) | |
| Unilateral IVH | 42 (10.1) | 34 (9.8) | 3 (33.3) | 5 (8.5) | |
| Bilateral IVH | 42 (10.1) | 28 (8.1) | 1 (11.1) | 13 (22.0) | |
| Transfusion Unit, mean ± SD (Range) | 1.17 ± 2.46 (0-21) | 0.67 ± 1.64 (0-10) | 6.89 ± 6.17 (1-21) | 3.29 ± 3.28 (0-11) | <0.001b |
| Ventilation Days, mean ± SD (Range) | 36 (8.7) | 9 (2.6) | 41.56 ± 37.02 (7-101) | 18.47 ± 17.82 (0-67) | <0.001b |
| PDA, n (%) | 36 (8.6) | 9 (2.6) | 6 (66.7) | 21 (35.6) | <0.001a |

[a] Chi Square Test was used for analysis of categorical variables

[b] One-Way ANOVA was used for analysis of continuous variables

***Table 4:*** *Binary Logistic Regression Analysis Of Different Variables To Predict severe ROP.*

**Model 1**

| | B | Sig. | Odd Ratio. | 95% C.I.for EXP(B) | |
|---|---|---|---|---|---|
| | | | | Lower | Upper |
| Ventilation (days) | 0.044 | 0.028 | 1.045 | 1.005 | 1.086 |
| Race | -1.242 | 0.020 | 0.289 | 0.101 | 0.823 |
| Head Scan Result | 0.639 | 0.038 | 1.895 | 1.035 | 3.471 |
| GA | -0.389 | 0.002 | 0.678 | 0.530 | 0.868 |
| Unit Of Transfusion | 0.021 | 0.853 | 1.021 | 0.821 | 1.270 |

**Model 2**

| | B | Sig. | Odd Ratio | 95% C.I.for EXP(B) | |
|---|---|---|---|---|---|
| | | | | Lower | Upper |
| GA | -0.443 | 0.000 | 0.642 | 0.501 | 0.823 |
| Unit Of Transfusion | 0.187 | 0.021 | 1.205 | 1.028 | 1.413 |
| Head Scan Result | 0.498 | 0.090 | 1.645 | 0.926 | 2.924 |
| Race | -1.236 | 0.017 | 0.291 | 0.105 | 0.805 |

**Model 3**

| | B | Sig. | Odd Ratio | 95% C.I.for EXP(B) | |
|---|---|---|---|---|---|
| | | | | Lower | Upper |
| BPD | 1.131 | 0.027 | 3.099 | 1.134 | 8.468 |
| Unit Of Transfusion | 0.321 | 0.000 | 1.378 | 1.201 | 1.580 |
| Head Scan Result | 0.545 | 0.067 | 1.725 | 0.963 | 3.092 |
| Race | -1.343 | 0.010 | 0.261 | 0.094 | 0.724 |

In East Lancashire Hospital NHS Trust, we serve an estimated population of 461,866, with an average of 6,000 life births per year [21]. Approximately 376,182 (81.4%) of the population are Caucasian, 77,615 (16.8%) are Asian (Pakistani, Indian, Bangladeshi, Chinese) and 8,069 (1.7%) others [21]. With 40 Caucasian ROP infants, they make up approximately 0.01% of the population, whereas 30 Asian ROP infants make up about 0.03% of the population. This makes Asian infants more likely to develop ROP as compared to Caucasian in our region. With the higher rates of consanguineous marriages and a degree of genetic relatedness among the Asian community in East Lancashire, the possibility of genetic susceptibility of ROP should be considered. A retrospective observational study published by Aralikatti et al. in 2009 compared ethnicity to those with threshold ROP (Stage 3 ROP with plus disease at Zone 1 and 2) [22]. They concluded that Asian and Afro-Caribbean infants were at higher risk of developing threshold ROP. Our study has further contributed to their finding, as we have found that Asian ethnicity are at more risk of developing stage 2 and 3 ROP and are more likely to require treatment (Table 4).

Our data shows correlation between laterality of IVH and ROP (Bilateral IVH is associated with higher ROP stages). The pathophysiology of IVH is interrelated to ROP. Similar to ROP, the incidence of IVH has an inverse correlation with GA. IVH is multifactorial and is dependent on anatomical factors like fragility of germinal matrix blood vessels and scarcity of pericytes, physiological factors (alteration of cerebral blood flow, impaired autoregulation and increased cerebral venous pressure) and neonatal comorbidities (PDA, mechanical ventilation, sepsis and hypercapnia) [23]. Likewise, ROP is contributed to by the deficiency in factors essential for retinal blood vessel development (i.e. insulin-like growth factor 1), impaired autoregulation and excessive supplemental oxygen and oxygen regulated pro-angiogenic and pro-inflammatory factors [24].

There are certain limitations to this study. The retrospective nature of this review can introduce bias and missing data, although measures have been taken to minimise this. Secondly, the number of ROP patients requiring treatment (Table 3) is small, thus statistical differences may be underestimated. Inter-rater variation in retinal examination in this study was minimised by only involving a single experienced ophthalmologist.

## Conclusion

Our paper shows that unilateral IVH is more common in premature infants with no ROP, whereas bilateral IVH is more common in ROP at all stages. Bilateral IVH is also associated with higher stages of ROP, and those requiring treatment. We also found a significant association between the amount of blood transfusion and severe ROP requiring treatment. Similarly, BPD is associated with higher stages of ROP. Furthermore, Asian infants are more likely to develop higher stages of ROP as compared to Caucasian infants.

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