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Neonatal Risk Factors Associated With Retinopathy of Prematurity

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ABSTRACT

Background: Retinopathy of prematurity, or ROP, is one of the major causes of childhood blindness. Most cases of ROP occur in premature infants, and several neonatal and demographic factors have been linked to the disease, although their relative importance is still being investigated. Knowledge regarding these risk factors is needed to produce effective prevention and treatment plans. This study aimed to identify neonatal risk factors linked to ROP.

Methodology: A case-control study was conducted at the Institute of Ophthalmology, Mayo Hospital Lahore. A total of 94 premature infants, with a gestational age of 37 weeks or less and a birth weight of ≤2500 g, were included, comprising 47 cases and 47 controls. Both groups were matched for age and gender. Data relating to gestation age, birth weight, and neonatal risk factors (neonatal sepsis, oxygen supplementation, blood transfusion, mechanical ventilation, respiratory infection history, ROP family history, multiple gestation) was ascertained on the questionnaire and subjected to Statistical Package for Social Sciences (SPSS) version 26.0 analysis.

Results: Significant risk factors in the study for developing ROP were multiple gestations, blood transfusions, and a family history of ROP with an adjusted odds ratio of 5.27, 9.11, and 12.92, respectively. Phototherapy was a protective factor (adjusted odds ratio = 0.28). The logistic regression model has a relatively good predictive ability with an AUC of 0.746.

Conclusion: This study highlights that multiple gestation, blood transfusion, and a family history of ROP significantly increase the chances of ROP development among premature infants, while phototherapy appears to offer a protective effect. These findings point out the importance of close monitoring and focused therapies for high-risk infants to avoid ROP development.

Keywords: *Retinopathy of Prematurity (ROP), Neonatal Risk Factors, Multiple Gestation, Blood Transfusion, Phototherapy, Family History*

1. INTRODUCTION

Retinopathy of prematurity (ROP) is a vasoproliferative disease of the preterm infant retina and remains one of the most common causes of child blindness in the world [1]. Vasculature of the retina develops during pregnancy (16 weeks) and ends at term. ROP is a 2 stage condition where retinal arteries of preterm neonates exposed to high oxygen at birth arrest initially, and then mature neovascular endothelial upregulation appears. Consecutive hypoxia increases the risk of neovascularization [2]. Most of the research across time estimates that ROP has an incidence of about 60% for premature newborns with a BW < 1500 g [3]. Stages of ROP have been reported in 40–50% of infants delivered at less than 30th week of gestation, severe ROP takes place in 7–8%, and 5–6% required treatment [4]. The latest study reported the frequency of ROP in Pakistan varies from 10.5% to 24.6% [5,6]. The development and progression of ROP involve contributions from many neonatal risk factors. The unique nature of ROP as being biologically multifaceted, due to differing gestational age, birth weight, and neonatal comorbidities as well as medical treatments, including oxygen supplementation and blood transfusions, emphasizes the need to define specific ROP risk profiles[7].

A recently published study found that RBC transfusion is an independent risk factor for ROP, particularly in young preterm infants. RBC transfusion was associated with ROP in the group with gestational age (GA) ≤32 weeks (OR = 1.77, 95% CI: 1.29–2.43) according to subgroup analysis [8]. Boskabadi et al. found that higher bilirubin levels in preterm may protect against the development of ROP. Phototherapy supports oxidative stress. Therefore, there is an apparent dilemma; on the one hand, serum-free bilirubin levels below or at certain values may be too high and provoke neurotoxicity, but retaining bilirubin levels at a modestly elevated concentration could be helpful because of the antioxidant effects of these compounds to stabilize cell membranes [9].

Neonates born in multiple gestation may have high-risk ROP, necessitating treatment at a more advanced gestational age and birth weight than singleton birth babies. Multiple birth neonates had significantly higher GA (27.50 ± 3.27 vs. 30.00 ± 2.00 vs. 31.14 ± 0.38 weeks, p = 0.032 for singletons, twins, and triplets, respectively) and BW (861.67 ± 274.62 vs. 1233.33 ± 347.75 vs. 1537.14 ± 208.86 g, $p = 0.002$), as per comparative examination of risk factors [10]. In another study, no difference was found between multiple-birth neonates and matched singletons regarding the incidence or severity of ROP [11].

Understanding these risk factors is critical for timely diagnosis, intervention, and prevention of severe ROP, which can have lifelong consequences for affected infants and their families. Although much has been done regarding research on the incidence of ROP in the last few decades, there still is disagreement as to which of these risk factors better indicates the development of ROP or the progression of different stages of the disease, not to mention its mechanisms of causing varying degrees of severity and the time of onset of ROP. The current study is designed to determine neonatal risk factors associated with Retinopathy of prematurity. Studying Retinopathy of Prematurity risk factors in Pakistan is crucial due to its impact on premature infants' vision. With a high rate of preterm births, understanding factors like gestational age, birth weight, oxygen use, and other neonatal influences is essential for early detection and intervention. This research aims to improve prevention and management strategies. By assessing these risk factors, healthcare providers can develop better guidelines and reduce ROP severity in premature infants in Pakistan and similar resource-limited settings globally.

2. MATERIALS AND METHODS

Study design*:* Case-control study

Place of study: Paeds Department, Institute of Ophthalmology Mayo Hospital, Lahore.

Sample selection criteria

Inclusion criteria

Case: Neonates born with gestational age 37 weeks or less, Birth weight ≤2500 g, and were diagnosed as having ROP; it was defined when abnormal blood vessels was seen in the retina (the light-sensitive layer of tissue in the back of the eye).

Control: Age-matched, sex-matched to a case, with normal vision

Exclusion criteria

- With congenital ocular anomalies
- Severe systemic diseases such as jaundice, multiple sclerosis, etc.
- Neonates whose parents had cousin marriage
- Neonates born to mothers under the age of 18 or over 40 years old were excluded
- Mothers with pre-existing health conditions such as hypertension, diabetes, or preeclampsia were excluded
- Neonates from families with a known genetic predisposition to ROP or other retinal disorders were excluded to eliminate any genetic influences.

Sampling technique and procedure

Non-probability convenient sampling where a group ratio of 1:1

Sample size: Sample size was estimated as a minimum of 47 cases and the same number of controls (1:1). Using P1= Mechanical ventilation =78.6% (in cases) [12] and P2= Mechanical ventilation = 50% (in controls) [12], at Power of test= 80% and Confidence level= 95%

Data collection procedure

Data collection was conducted after obtaining approval from the Research Ethics Committee of the University of Lahore (REC# 487/24). The Institute of Ophthalmology, Mayo Hospital administration facilitated data collection. Informed consent was obtained from parents or attendants before data collection. All information on birth weight, gestational age, and neonatal risk factors (such as neonatal sepsis, days on oxygen, and blood transfusion) was recorded in a questionnaire for analysis.

Incomplete forms were excluded, and only complete data was entered into SPSS version 26. Retinopathy of Prematurity (ROP) was defined as the abnormal growth of blood vessels in the retina, the light-sensitive layer at the back of the eye. Data regarding birth weight, gestational age, blood transfusion, oxygen therapy, multiple gestation, neonatal anemia, mechanical ventilation, and steroid use during the hospital stay were gathered from medical records or confirmed with parents/attendants.

Data was analyzed using SPSS version 26. Frequencies and percentages were calculated for categorical variables, while means, standard deviations, median, and interquartile range (IQR) were used for continuous variables. The Kolmogorov-Smirnov test was used to assess the normality of the data, which confirmed that birth weight, gestational age, and birth order were not normally distributed. To identify risk factors, univariate analysis was conducted. The Pearson $\chi 2$ test was applied to categorical variables, and the Mann-Whiten test was applied to numerical variables. For multivariate logistic regression, variables were selected from univariate analysis where the p-value was ≤ 0.2. Logistic regression coefficient, i.e., β, p-value (Wald test), unadjusted and adjusted Odds ratio (OR) were presented along with a 95% confidence level. Receiver operating characteristic (ROC) and area under the curve were reported. A p-value ≤ 0.05 was considered statistically significant.

3. RESULTS

The comparison of demographic and neonatal risk factors between ROP cases and controls reveals several significant differences. The distribution of gender was identical between cases and controls, with females comprising 26(55.3%) and males 21(44.7%) in both groups ($p = 1.000$). The mean gestational age for cases was 30.13 ± 3.09 weeks, and for controls, it was 30.74 ± 3.02 weeks. The median gestational ages were 31 weeks (IQR = 4) for cases and 32 weeks (IQR = 5) for controls, showing no significant difference ($p = 0.322$). The mean birth weight for cases was 1643.62 ± 633.02 g, compared to 1587.23 ± 341.11 g for controls. Both groups had a median birth weight of 1500 g, but the interquartile range was wider for cases (800) compared to controls (600), with no significant difference ($p = 0.612$).

The mean birth order was similar between cases (2.23 ± 1.24) and controls (2.15 ± 1.32). The median birth order was 2 for both groups (IQR = 2), with no significant difference ($p = 0.632$). Among cases, 17(36.2%) had underdeveloped lungs compared to 13(27.7%) among controls ($p = 0.376$). Oxygen therapy was administered to 42(89.4%) of the cases and 44(93.6%) of the controls, with no significant difference ($p = 0.460$). A significantly higher proportion of cases 16(34.0%) were from multiple gestations compared to controls 4(8.5%) ($p = 0.002$). Sepsis was present in 22(46.8%) of the cases and 21(44.7%) of the controls, with no significant difference ($p = 0.836$). Anemia was significantly more common in cases 32(68.1%) than in controls 15(31.9%) ($p < 0.001$).

RDS was present in 32(68.1%) of the cases and 36(76.6%) of the controls, with no significant difference ($p = 0.356$). Steroid use was noted in 40(85.1%) of the cases and 35(74.5%) of the controls, with no significant difference ($p = 0.199$). Blood transfusion was significantly more common in cases 30(63.8%) compared to controls 11(23.4%) ($p < 0.001$). Mechanical ventilation was used in 19(40.4%) of the cases and 11(23.4%) of the controls, with no significant difference ($p = 0.077$). A family history of ROP was present in 9(19.1%) of the cases and 1(2.1%) of the controls, showing a significant difference ($p = 0.007$). History of respiratory infections was significantly more common in cases 36(76.6%) than in controls 25(53.2%) ($p = 0.017$). Phototherapy was administered to 33(70.2%) of the cases and 38(80.9%) of the controls, with no significant difference ($p = 0.230$). More details can be found in Table 1

In the multivariate logistic regression analysis, several factors were identified as significant predictors of ROP. Multiple gestations were a significant predictor, with an adjusted odds ratio (aOR) of 5.27 [1.31, 21.19] ($p = 0.02$). Blood transfusion was another significant predictor, with an aOR of 9.11 [3.02, 27.42] ($p < 0.001$). A family history of ROP showed a significant association, with an aOR of 12.92 [1.11, 150.73] ($p = 0.04$). Phototherapy was found to be a protective factor, with an aOR of 0.28 [0.08, 0.93] ($p = 0.04$). The logistic model is given by the equation: $\text{logit}(y) = -0.49 + 1.66 \times (\text{multiple gestation}) + 2.21 \times (\text{blood transfusion}) + 2.56 \times (\text{family history of ROP}) - 1.27 \times (\text{phototherapy})$. Refer to Table -2 for more details. The Area Under the Curve (AUC) for the logistic model was 0.746 (SE = 0.052, $p < 0.001$), with a 95% confidence interval of 0.644 to 0.847, as shown in Table 3, indicating a good predictive performance of the model.

4. DISCUSSION

One of the leading causes of visual loss in children worldwide is retinopathy of prematurity (ROP) [13]. Only preterm children are prone to retinal blood vessel disease, commonly referred to as retinopathy of prematurity (retinopathia praematurorum, or ROP). Most children suffer from mild ROP, which means that the disease self-resolves. However, more severe forms of ROP can lead to blindness in one or both eyes [14].

The risk factors of ROP are diverse, including, comprising maternal, prenatal, and perinatal risk factors, demographic characteristics, treatment of medical and dietary conditions, and genetics. Most traditional factors include a low birth weight, low GA, and higher levels of unstable oxygen at the time of birth or shortly thereafter. The risk of severe ROP increases with decreasing BW and GA. Variations in oxygen levels throughout the newborn period and intermittent hypoxia (SpO2 <80% for 1 minute or longer) have also been found to be risk factors for ROP. [15]

Smaller BW, perinatal morbidities, and an increased risk of preterm delivery are linked to multiple gestations, and these

factors may influence the risk of ROP. With this, ROP was more likely to occur in babies who were delivered as twins or with low birth weight. In newborns who have low birth weight and have undergone artificial breathing, extreme caution coupled with constant observation is necessary. According to a retrospective comparative study, neonates who were born as part of multiple births (either twins or triplets) were, at a higher risk of being subjected to the treatment for ROP, and differed in gestational age, birth weight, and oxygen supplementation or length of stay in NICU [16]. The incidence rate of ROP in the twin group was 13.6 times higher than that of the singleton cohort, with a ratio of 35.1 to 2.58 per 10,000 person-years; adjusted HR = 13.4, 95% CI = 11.7–15.3; p<0.0001, according to a study conducted by Tseng H-C et al [17]. In a similar manner, a Turkish study found that newborns with a history of numerous pregnancies had considerably greater ROP development. Multivariable analysis revealed a significant correlation between the development of ROP and multiple pregnancies (β=2.375, p=0.001) [18].

The findings from our study are coherent with those of previous studies. This study indicated a significantly higher proportion of cases from multiple gestations compared to controls (p = 0.002). Moreover, multiple gestations emerged as a significant predictor in study, with an adjusted odds ratio (aOR) of 5.27 [1.31, 21.19] (p = 0.02).

The risk of ROP increases with the increasing volume of blood and the RBC transfusions. In a study conducted by Ghirardello et al., 641 preterm children with extremely low birth weights showed an increase in the incidence of ROP by 4.88 times with an increase in the number of transfusions [19]. From a prospective multicenter cohort research, the risk of ROP was much greater in the transfusion group; (P=.009) [20]. In a parallel fashion, another retrospective cohort research suggested the odds of ROP were at 3.95 times following adjustment for the oxygen treatment and GA and 2.77 fold after having greater transfusions [21]. According to observational research, blood transfusion was found to be substantially associated with ROP development [22].

Although the precise mechanism whereby RBC transfusion induces the development of ROP remains to be unknown, it is perhaps related to the nature and amount of haemoglobin changed at the time fetal haemoglobin (HbF) is exchanged with adult haemoglobin following transfusion. Adult haemoglobin has a low affinity for oxygen, so if growing retinal tissue is subjected to high levels of oxygen, the vascular endothelial cells suffer oxidative damage and VEGF expressions are suppressed, retinal vascular development remains stagnant, and ROP develops [23]. This was further supported by an observational, prospective study that indicated a higher percentage of HbF was associated with a lower incidence of ROP. In contrast, the replacement of adult haemoglobin during blood transfusions may promote the development of ROP [22].

One possible reason would be that a transfusion produces reactive oxygen species, which stimulate excessive oxidative damage leading to ROP. The level of blood transfusions influences which stage of this disease of premature newborns suffers the most progression. Newborns with anemia (Hgb ≤ 8 g / dl or Hct ≤ 25%) suffered mild ROP comparatively to newborns with less intense anemia [24]. According to one study, ROP was significantly correlated with the number of blood transfusions that occurred during the first week of life, leading to a tremendous cumulative volume [25].

These findings align with this study, which showed that there is a significant association of blood transfusion with Retinopathy of Prematurity having an aOR of 9.11 [3.02, 27.42], (p < 0.001) and neonatal anemia is also a significant indicator of ROP(p < 0.001). The aOR of 9.11 in this study is notably higher than those reported in the other studies, possibly due to differences in population characteristics. In our study, Anemia (p= <0.001) is significantly associated with Retinopathy of prematurity. The study reinforces the findings of previous research, indicating a strong link between anemia, blood transfusions, and an increased risk of retinopathy of prematurity. Both anemia (p<0.001) and blood transfusions (p<0.001) were significantly associated with ROP in the study. This result is consistent with many other reports.

Numerous studies have confirmed that genetic elements play vital role in ROP phenotypic variability. Many recent studies have successfully identified candidate genes from various pathways of signaling molecules involved in ROP development. When environmental factors were included, a significant genetic contribution to ROP was demonstrated in a recent twin study that compared the prevalence of ROP in monozygotic and dizygotic twin pairs [26]. ROP may be influenced by genetic risk factors, as described in research conducted at the University of Iowa Children's Hospital [27]

However, according to the results of another study, the development of ROP was not significantly related to clinically recognized risk factors in PTI with severe morphologies. This indicates that some other clinical, maternal, or genetic factors either predispose to or protect against ROP [28]. In this study, a family history of ROP was present in 9(19.1%) of the cases and 1(2.1%) of the controls, showing a significant difference (p = 0.007). A family history of ROP showed a significant association, with an aOR of 12.92 [1.11, 150.73] (p = 0.04). This supports the importance of genetic variables and agrees with twin studies that showed a heritability factor of 0.73 for ROP [29].

RDS is a respiratory illness that occurs in preterm infants and is induced by the deficiency of surfactants in the lungs. Besides having increased oxygenation, RDS may also cause hyperoxemia in the developing retina, which prevents the formation of retinal vessels. ROP may thus be a result of the subsequent hypoxia of the retina. One study indicated that RDS and the onset of ROP were highly associated [3]. Another research revealed that the aHR was 1.28 (95% CI = 1.18–1.39) 30, and the incidence of ROP was 2.5 times greater in RDS children than in control (30.3 versus 11.9 per 100 person-years) [30]. However,

in our study result RDS was present in 32(68.1%) of the cases and 36(76.6%) of the controls, with no significant difference (p = 0.356). The results are inconsistent due to small population size and epidemiological variations.

Babies with apnea have a higher risk of developing ROP and will require more mechanical ventilation and more oxygen. The lowest and highest FiO2 values were obtained in babies whose ROP was developing and progressing, and the average time spent on oxygen therapy was much longer. It has been found that the onset and progression of ROP are associated with the duration of assisted breathing. Similarly, a higher risk of ROP development and progression is related to the requirement for ventilator support and/or oxygen at 36 weeks, which implies moderate/severe BDP. Babies may require oxygen therapy and artificial breathing since a lack of surfactants causes RDS. Thus, a higher incidence of ROP is related to RDS. ROP incidence is 2.5 times more in RDS children as compared to controls [31]

Phototherapy is one recommended treatment for neonatal hyperbilirubinemia and exposes newborns to light. It remains a crucial intervention in the treatment of severe hyperbilirubinemia, especially for high-risk neonates, which include preterm newborns [32]. In a study, of the total number of 60 newborns treated under phototherapy, 15 developed ROP. ROP development wasn't significantly affected by phototherapy (p = 0.688) [33]. However, as shown in another study, there is a higher likelihood of developing ROP if one has hyperbilirubinemia that requires phototherapy [34]. Strikingly, a contemporary study found that high bilirubin levels in newborns are associated with less severe ROP and might even be a protective factor against ROP [9]. These findings emphasize the complex and inconsistent relationship between bilirubin, phototherapy, and ROP. In this study, the phototherapy was found to be a protective factor, with an aOR of 0.28 [0.08, 0.93] (p = 0.04). Therefore, prophylaxis phototherapy in premature infants may need to be reconsidered. According to some studies, surfactant therapy is significantly associated with ROP, and this may be an indicator that neonates treated with phototherapy for jaundice are more susceptible to developing ROP. According to our study, surfactant therapy was almost universal in preterm infants, both in the case and control groups, and it had no apparent association with preterm birth retinopathy.

Table 1: Comparison of demographic and neonatal risk factors for ROP

		ROP		Test	p-value
		Control	Case		
Gender	Female (n%)	26(55.3%)	26(55.3%)	<0.0001[a]	1.000
	Male(n%)	21(44.7%)	21(44.7%)		
Gestational Age (weeks)	Mean ± S.D	30.74± 3.02	30.13± 3.09	-0.991[b]	0.322
	Median (IQR)	32 (5)	31 (4)		
Birth Weight (g)	Mean ± S.D	1587.23± 341.11	1643.62± 633.02	-0.498 [b]	0.612
	Median (IQR)	1500 (600)	1500 (800)		
Birth Order	Mean ± S.D	2.15± 1.32	2.23± 1.24	-0.479 [b]	0.632
	Median (IQR)	2 (2)	2 (2)		
Lungs not developed	No(n%)	34(72.3%)	30(63.8%)	0.783 [a]	0.376
	Yes(n%)	13(27.7%)	17(36.2%)		
Oxygen Therapy	No(n%)	3(6.4%)	5(10.6%)	0.547 [a]	0.460
	Yes(n%)	44(93.6%)	42(89.4%)		
Multiple gestations	No(n%)	43(91.5%)	31(66.0%)	9.146 [a]	0.002*
	Yes(n%)	4(8.5%)	16(34.0%)		
Sepsis/ infection	No(n%)	26(55.3%)	25(53.2%)	0.043 [a]	0.836
	Yes(n%)	21(44.7%)	22(46.8%)		
Neonatal Anemia	No(n%)	32(68.1%)	15(31.9%)	12.298 [a]	<0.001**
	Yes(n%)	15(31.9%)	32(68.1%)		
Respiratory Distress Syndrome	No(n%)	11(23.4%)	15(31.9%)	0.851 [a]	0.356
	Yes(n%)	36(76.6%)	32(68.1%)		
Steroid use	No(n%)	12(25.5%)	7(14.9%)	1.649 [a]	0.199
	Yes(n%)	35(74.5%)	40(85.1%)		

Blood transfusion	No(n%)	36(76.6%)	17(36.2%)	15.616 [a]	<0.001**
	Yes(n%)	11(23.4%)	30(63.8%)		
Mechanical ventilation	No(n%)	36(76.6%)	28(59.6%)	3.133 [a]	0.077
	Yes(n%)	11(23.4%)	19(40.4%)		
Family history of ROP	No(n%)	46(97.9%)	38(80.9%)	7.172 [a]	0.007*
	Yes(n%)	1(2.1%)	9(19.1%)		
History of Respiratory Infections	No(n%)	22(46.8%)	11(23.4%)	5.670 [a]	0.017*
	Yes(n%)	25(53.2%)	36(76.6%)		
Phototherapy for jaundice	No(n%)	9(19.1%)	14(29.8%)	1.439 [a]	0.230
	Yes(n%)	38(80.9%)	33(70.2%)		

***| Highly Significant, *| Significant, a| Chi-square test was applied, b| Maan Whiteny U test was applied*

Table 2: Multivariate analysis of risk factors of ROP

	β	**p-value**	**Unadjusted OR [95% CI]**	**β**	**p-value**	**Adjusted OR [95% CI]**
Birth. Order	-0.21	0.34	0.81[0.52, 1.25]			
Lung's not developed	0.43	0.64	1.54[0.25, 9.39]			
Oxygen therapy (yes)	0.43	0.73	1.54[0.13, 18.60]			
Multiple gestations (yes)	2.21	0.01	9.14[1.65, 50.49]	1.66	0.02	5.27 [1.31, 21.19]
Sepsis (yes)	-0.58	0.42	0.56[0.14, 2.32]			
Anemia (yes)	0.50	0.57	1.65[0.29, 9.50]			
RDS (yes)	-0.88	0.43	0.41[0.05, 3.65]			
Steroid use (yes)	1.77	0.08	5.89[0.81, 42.89]			
Blood Transfusion (yes)	1.85	0.03	6.37[1.26, 32.27]	2.21	<0.001	9.11 [3.02, 27.42]
Mechanical Ventilation (yes)	-0.01	0.99	0.99[0.21, 4.64]			
Family History of ROP (yes)	2.35	0.10	10.49[0.65, 169.71]	2.56	0.04	12.92 [1.11, 150.73]
Respiratory infection (yes)	0.64	0.38	1.89[0.46, 7.74]			
Phototherapy (yes)	-2.20	0.01	0.11[0.02, 0.55]	-1.27	0.04	0.28 [0.08, 0.93]
Constant	-0.89	0.52	0.41	-0.49	0.35	0.614

RDS| Respiratory distress syndrome, OR| Odds ratio

Table 3: Area Under the Curve

Area	Std. Error [c]	p-value [d]	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
0.746	0.052	<0.001	0.644	0.847

c| Under the nonparametric assumption, d| Null hypothesis: true area = 0.5

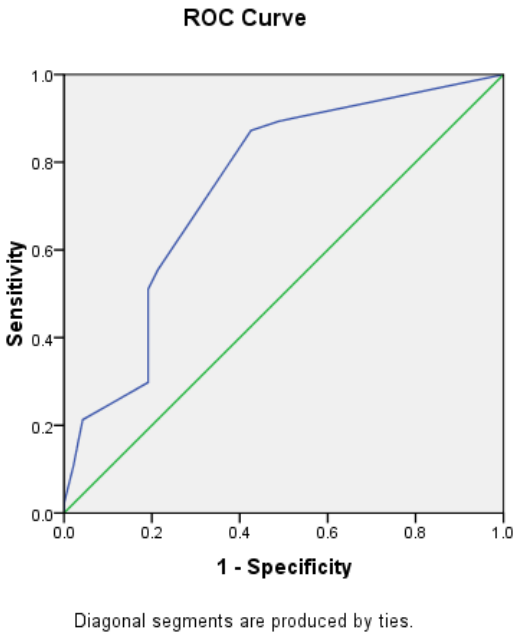

Figure-1: Receiver operating characteristic

REFERENCES

[1] Tl T. Extreme prematurity and fibroblastic overgrowth of persistent vascular sheath behind each crystalline lens. I. Preliminary report. Am J Ophthalmol. 1942;25:203-4.

[2] de las Rivas Ramírez N, Luque Aranda G, Rius Díaz F, Pérez Frías FJ, Sánchez Tamayo T. Risk factors associated with Retinopathy of Prematurity development and progression. Sci Rep. 2022;12(1):21977.

[3] Chang JW. Risk factor analysis for the development and progression of retinopathy of prematurity. PLoS ONE. 2019;14(7):e0219934.

[4] Jefferies AL, Society CP, Fetus, Committee N. Retinopathy of prematurity: An update on screening and management. Paediatr Child Health. 2016;21(2):101-4.

[5] Hanif M, Ariff S, Ansar A, Ahmed K, Hussain AS. Characteristics of preterm with sight threatening retinopathy of prematurity. JAMC. 2020;32(2):174-8.

[6] Ali AA, Gomaa NA, Awadein AR, Al-Hayouti HH, Hegazy AI. Retrospective cohort study shows that the risks for retinopathy of prematurity included birth age and weight, medical conditions and treatment. Acta Paediatr. 2017;106(12):1919-27.

[7] Kim SJ, Port AD, Swan R, Campbell JP, Chan RP, Chiang MF. Retinopathy of prematurity: a review of risk factors and their clinical significance. Surv Ophthalmol. 2018;63(5):618-37.

[8] Zhu Z, Hua X, Yu Y, Zhu P, Hong K, Ke Y. Effect of red blood cell transfusion on the development of retinopathy of prematurity: A systematic review and meta-analysis. Plos One. 2020;15(6):e0234266.

[9] Boskabadi H, Shoeibi N, Bagheri F, Pourbadakhshan N, Moradi A, Zakerihamidi M. Potential role of bilirubin in preventing retinopathy of prematurity. Curr Pediatr Rev. 2023;19(2):197-202.

[10] Johari M, Karimi A, Mojarad M, Heydari M. Comparative analysis of risk factors for retinopathy of prematurity in single and multiple birth neonates. Int J Retina Vitreous. 2024;10(1):21.

[11] Riazi-Esfahani M, Alizadeh Y, Karkhaneh R, Mansouri M-R, Kadivar M, Ahmadabadi MN, et al. Retinopathy of prematurity: single versus multiple-birth pregnancies. JOVR. 2008;3(1):47.

[12] Onyango O, Sitati S, Amolo L, Murila F, Wariua S, Nyamu G, et al. Retinopathy of prematurity in Kenya: prevalence and risk factors in a hospital with advanced neonatal care. Pan African Medical Journal. 2018;29(1):1-7.

[13] Solebo AL, Teoh L, Rahi J. Epidemiology of blindness in children. Arch Dis Child. 2017;102(9):853-7.

[14] Alajbegovic-Halimic J, Zvizdic D, Alimanovic-Halilovic E, Dodik I, Duvnjak S. Risk factors for retinopathy of prematurity in premature born children. Med Arch. 2015;69(6):409.

[15] Sabri K, Ells AL, Lee EY, Dutta S, Vinekar A. Retinopathy of prematurity: a global perspective and recent developments. Pediatrics. 2022;150(3).

[16] Johari M, Karimi A, Mojarad M, Heydari M. Comparative analysis of risk factors for retinopathy of prematurity in single and multiple birth neonates. IJRV. 2024;10(1):21.

[17] Tseng H-C, Sung F-C, Mou C-H, Lin HY, Chiang C-C, Hsia N-Y, et al. Population based retrospective cohort study on risk of retinopathy of prematurity in twins. Plos One. 2020;15(3):e0230346.

[18] YENİCE EK, KARA C. Development of Retinopathy of Prematurity in Late Preterm Infants: Singleton or Multiple Pregnancies: Observational and Descriptive Research. Turkiye Klinikleri J Ophthalmol. 2024;33(1):30-5.

[19] Ghirardello S, Dusi E, Cortinovis I, Villa S, Fumagalli M, Agosti M, et al. Effects of red blood cell transfusions on the risk of developing complications or death: an observational study of a cohort of very low birth weight infants. Am J Perinatol. 2017;34(01):88-95.

[20] Wang X, Rao R, Li H, Lei X, Dong W. Red Blood Cell Transfusion for Incidence of Retinopathy of Prematurity: Prospective Multicenter Cohort Study. JMIR Pediatr Parent. 2024;7:e60330.

[21] Uberos J, Fernandez-Marin E, Campos-Martínez A, Ruiz-López A, García-Serrano JL. Blood products transfusion and retinopathy of prematurity: A cohort study. Acta Ophthalmol. 2023;101(3):e294-e301.

[22] Prasad N, Kumar K, Dubey A. Fetal hemoglobin, blood transfusion, and retinopathy of prematurity in preterm infants: An observational, prospective study. Indian J Ophthalmol. 2023;71(7):2803-7.

[23] Podraza W. A new approach to neonatal medical management that could transform the prevention of retinopathy of prematurity: theoretical considerations. Med Hypotheses. 2020;137:109541.

[24] Englert JA, Saunders RA, Purohit D, Hulsey TC, Ebeling M. The effect of anemia on retinopathy of prematurity in extremely low birth weight infants. Journal of Perinatology. 2001;21(1):21-6.

[25] Hesse L, Eberl W, Schlaud M, Poets C. Blood transfusion: iron load and retinopathy of prematurity. European journal of pediatrics. 1997;156:465-70.

[26] Bizzarro MJ, Hussain N, Jonsson B, Feng R, Ment LR, Gruen JR, et al. Genetic susceptibility to retinopathy of prematurity. Pediatrics. 2006;118(5):1858-63.

[27] Mohamed S, Schaa K, Cooper ME, Ahrens E, Alvarado A, Colaizy T, et al. Genetic contributions to the development of retinopathy of prematurity. Pediatric research. 2009;65(2):193-7.

[28] Port AD, Chan RP, Ostmo S, Choi D, Chiang MF. Risk factors for retinopathy of prematurity: insights from outlier infants. Graefes Arch Clin Exp Ophthalmol. 2014;252:1669-77.

[29] Ortega-Molina J, Anaya-Alaminos R, Uberos-Fernández J, Solans-Pérez de Larraya A, Chaves-Samaniego M, Salgado-Miranda A, et al. Genetic and environmental influences on retinopathy of prematurity. Mediators Infamm. 2015;2015(1):764159.

[30] Lin Y-W, Chen S-N, Muo C-H, Sung F-C, Lin M-H. Risk of retinopathy of prematurity in preterm births with respiratory distress syndrome: a population-based cohort study in Taiwan. Int J Gen Med. 2022:2149-62.

[31] Lin Y-W, Chen S-N, Muo C-H, Sung F-C, Lin M-H. Risk of retinopathy of prematurity in preterm births with respiratory distress syndrome: a population-based cohort study in Taiwan. International Journal of General Medicine. 2022:2149-62.

[32] Bhutani VK, Wong RJ, Turkewitz D, Rauch DA, Mowitz ME, Barfield WD, et al. Phototherapy to Prevent Severe Neonatal Hyperbilirubinemia in the Newborn Infant 35 or More Weeks of Gestation: Technical Report. Pediatrics. 2024;154(3).

[33] Kumar PS, Kannan KS, Arunarani R, Ramaswami M, Esther R. A STUDY ON THE RISK FACTORS OF RETINOPATHY OF PREMATURITY. Int J Acad Med Pharm. 2023;5(2):1008-13.

[34] Gulden S, Cervellini G, Colombo M, Marangoni MB, Taccani V, Pesenti N, et al. Hyperbilirubinemia and retinopathy of prematurity: a retrospective cohort study. Eur J Pediatr. 2024:1-10.