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Evaluation of Risk Factors for Retinopathy of Prematurity in Premature Born Infants in Tertiary Care Centre in Punjab

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Abstract

Background: Retinopathy of Prematurity (ROP) is a disease where development of abnormal retinal vessels occurs because of incomplete vascularization of the retinal tissue. With advancement in the field of neonatology now more premature babies and Very-Low-Birth-Weight (VLBW) infants surviving and incidence of retinopathy of prematurity is increasing. ROP screening should be done in all premature babies. **Objectives:** To Study the Risk Factors for Retinopathy of Prematurity in Premature Born infants at tertiary care centre. **Methods:** This study was done on 75 newborns infants and were included in study after satisfying the inclusion criteria. The following criteria were studied: gestational age≤34 weeks or BW≤1500 grams, along with neonates with more birth weight and higher gestational age having risk factors like : low Apgar score, duration of oxygen supplementation more than 10 days, sepsis, more than one blood transfusion, respiratory distress. Characteristics of newborns including risk factors, and pattern of severe ROP were assessed from Punjab region of India. **Result:** Total of 75 newborns included in the study, 53 were males (70.66%) and 22 were (29.33%) females. The analysis of gestational age showed that the mean age was 29.9±2.9 weeks, the youngest one was of 27 weeks and the oldest was 37 weeks of gestation. The average birth weight was 1350±510 grams, with lowest 675 gm and highest 3100 grams. **Conclusion:** The most common risk factors that are associated with development of ROP revealed gestational age, Apgar score in the first minute, birth weight, duration of oxygen therapy and the blood transfusion.

Keywords: Apgar Score, Continuous Pressure, Oxygen Duration, Respiratory Distress, CPAP

1. Introduction

Retinopathy of prematurity (ROP) is a disease where development of abnormal retinal vessels occurs because of incomplete vascularization of the retinal tissue due to hyperoxia leading to down regulation of VEGF and it is most commonly seen in premature infants. Majority infants show mild form of retinopathy of prematurity and the disease regresses spontaneously. But the disease may present in more severe forms leading to unilateral or bilateral blindness. With advancement in the field of neonatolgy now more premature babies and VLBW infants surviving and incidence of retinopathy of prematurity is increasing[1]. The first retinal changes described by Terry in 1942 in the survived premature babies is of fibrovascular bundles, Health in 1951

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introduced the term retinopathy of prematurity[2]. It is a usual finding in premature babies, but there are various risk factors with interactive effects[3]. Early gestation age i.e., ≤34 weeks and low birth weight i.e., ≤1500g are known risk factors for ROP, other factors associated with the ROP are poor weight gain, the percentage of oxygen and duration of oxygen which are important factors in development of ROP[4-7]. ROP is classified by International Classification of Retinopathy of Prematurity (ICROP), into three zones and five stages and additional risk factors & progression of ROP are categorised "plus disease"[8]. The three zones of ROP are centred on the optic disc. Zone I is the small circle of retina around the optic disc. The radius of the circle is twice the distance from the macula to the centre of the optic disc Zone II is the ring-shaped section of the retina surrounding zone I, which extends to the ora serrata on the nasal side Zone III is a crescent-shaped area of temporal retina. ROP in zone I is more likely to progress and become severe than ROP in zones II or III. Prethreshold ROP was defined as any zone 1 ROP less than threshold, zone 2 stage 2 with plus, zone 2 stage 3 without plus or zone 2 stage 3 with plus but less than 5 contiguous or less than 8 cumulative clock hours of ROP. It is very important that first examination of children who are <34 weeks of gestational age or have birth weight <1500 grams should be by an ophthalmologist during 3-4 weeks after birth. Time of initial examination is decided by postmenstrual age and chronological age both and is done to find out infants at risk of a poor visual outcome. A neonatologist asks for examination by ophthalmologist in premature infants having older gestational age, if risk factors are present. Future monitoring of these patients is by ophthalmologist[9].

Treatment of ROP targets the avascular part of the retina and main principal is retinal ablation aiming to decrease the growth factors leading to angiogenesis. Cryotherapy and laser photocoagulation are the methods preferred to decrease poor visual and structural outcomes of eyes[2]. Even after complete screening long-term follow up of premature children is required as there is increased incidence of other complications like retinal detachment, strabismus, glaucoma, etc[8-10].

This study was conducted to describe the characteristics including risk factors, and pattern of severe ROP from Punjab region of India.

2. Materials and Methods

This study was done in neonatal intensive care unit of Punjab Institute of medical sciences, Jalandhar, Punjab between Jan 2017 to Jan 2018 after getting approval from IEC. It included total 75 neonate out of which 5 were term neonate. The Criteria for ROP screening was done according to standard guidelines in neonates, and they were shortlisted for the ophthalmic examination. The following criteria were taken into account: Gestational age ≤34 weeks or BW ≤1500 grams. Neonate at higher gestational age and more birth weight with any of the risk factors like: Low Apgar score, duration of oxygen supplementation more than 10 days, sepsis, more than 1 blood transfusion, respiratory distress syndrome, use of surfactant, duration of ventilation, delivery by NVD and LSCS. First examination was conducted by the ophthalmologist in neonatal ICU and subsequent at the Eye OPD as planned by ophthalmologist based on the retinal blood vessel development. It was done almost every week, until the retinal blood network was completely developed. Examination of Neonates was done by using indirect ophthalmoscope with dilatation of pupil by Sol. Phenylephrine HCL 2.5% and 0.5% Sol. Cyclopentolate. The findings on fundus examination were: bleeding, ischemic zones, dilated and tortuous blood vessels, optic nerve changes and signs of "plus disease" and aggressive posterior ROP (AP-ROP). Infants with active ROP showed changes in vessels and suspicious ischemic zones requiring treatment by injection of anti-VEGF factors, laser photo coagulation or vitreoretinal surgery. Data were analyzed using software SPSS version 20. Qualitative variables were analyzed using Chi Square test and quantitative variables were analyzed using student t test. P value was calculated and a value<0.05 was considered as significant.

3. Results

Out of 75 newborns, 53 were males (70.66%) and 22 (29.33%) were females. The analysis of gestational age showed that the mean age was 29.9±2.9 weeks, the youngest was of 27 weeks and the oldest was of 37 weeks. Out of 75 newborns, the mean weight was 1350±500.5 grams, with lowest of 675 gm and highest of 3100 grams. (Table 1).

Analysis of gestational age indicates that patients who developed active ROP were statistically significantly born

Table 1. Demographic data

Male	53 (70.66%)
Female	22 (29.33%)
Surfactant	34
Mode of delivery LSCS/NVD	65/10
Antenatal steroid	40 (53.33%)
CPAP	59
Mean duration CPAP (hours)	173.2 +23.7
Mean duration of ventilation (hrs)	43.5 +9.7
Mean gestational age(weeks)	29.9 ± 2.9
Mean weight (gm)	1350.18 ± 500.5
Duration of oxygen in days	30.7+3.4

earlier or with mean GA of 28.5±2.1 weeks compared to those who did not develop active ROP–32.6±1.8 week. Also, birth weight was statistically significantly lower in patients who developed active ROP–950±150 grams compared to patients who did not develop active ROP–1647.18±760.7 grams. Patients who developed active ROP had statistically lower first minute Apgar score (3.8±1.1:5.92±1.5) and five-minute Apgar score (5.6±1.5:6.64±2.5) compared to those patients who did not develop active ROP patients with active ROP were given oxygen therapy for longer duration(30.7±3.4 days) in comparison to the patients who did not have active disease 10.5±1.1 days which was significant (p<0.0001). (Table 2).

Table 2. Comparison of various risk factors - Gestational age, birth Weight, Apgar score, oxygen therapy in newborns with active ROP and without ROP

	ROP (yes) 10 (Mean +SD)	ROP (No) 65(Mean +SD)	T	P value
Gestational Age (weeks)	28.5+2.1	32.6+1.8	2.813	0.0063
Birth wt. (grams)	950.0+150.5	1647.18+760.7	2.873	0.0053
Apgar Score (1min)	3.8+1.1	5.92+1.5	4.284	0.0001
Apgar Score (5min)	5.6+1.5	6.64+2.5	1.276	0.206
Duration of oxygen therapy (Days)	30.7+3.4	10.5+1.1	37.71	0.0001

Of the total 20 patients with sepsis 4(20%) cases had active ROP and 16(80%) patients with no pointers towards infection developed disease indicating no statistically significant relation with the development of active ROP. Out of 24 Blood transfusion 6(25.6%) cases developed active ROP and 18(75%) no ROP it shows a significant correlation. In Case of IVH 1(1.3%) developed active ROP and 15(2%) did not and it was not statically significant (Table 3).

Table 3. Analysis of risk factors

	Active	ROP		Total	X2	p
		Y	N			
Sepsis	Y	4	16	20	1.049	0.035
	N	6	49			
Blood transfusion	Y	6	18	24	4.157	0.041
	N	4	47			
RDS	Y	1	25	26	3.099	0.078
	N	9	40			
IVH	Y	1	15	16	0.883	0.347
	N	9	50			

Analysis of patients based on zones revealed that out of total number of patients (N = 75), zone I : 10 (13.33%) cases, zone II: 20 (26.66%) cases, and zone III: 45 (60%) cases. Only zone I patients had active disease, while zone II or III patients did not get active disease pointing towards impact of zones in the development of active disease (p<0.05) (Table 4).

Table 4. Active ROP and zones

Active ROP					
			Y	N	Total
Zone	1	N	10	0	10
	II	%	100.0	0.0	100.0
	III	N	0	20	20
		%	0	100.0	100.0
		N	0	45	45
		%	0	100	100.0
Total		N	10	65	75
		%	13.33	86.66	100

4. Discussion

In our study we observed 75 newborn who were selected for retinopathy of prematurity screening. There was

higher representation rate for male infants i.e., 53(70.66%) compared to female i.e. 22(29.33%). Average GA was 30.6±1.9 weeks. The gestational age of youngest infant was 27 wks and of the oldest infant was 37 wks. Birth weight average was 1350±515 gms ranging from 675 to 3100 gms. The active disease was seen in 10 (13.3%) patients who required anti-VEGF factors application, all 10 cases were treated with argon laser photocoagulation and one case was referred to PGI Chandigarh because of bleeding. Remaining 65(86.6%) cases had regressed spontaneously.

Zone I patients were the youngest i.e., 28.5±2.11 wks gestation and those in zone III were the oldest with 32.6±1.8 wks which was statistically significant. Lowest birth weight patients fell in zone I (950±150.5 grams) and the zone III patients had highest birth weight (1647.9±760.7 grams) which was significant statistically ($p<0.05$). Lowest first minute Apgar score was seen in zone I children (3.8±1.1) and zone III patients had the highest score (5.92±1.8) which was significant statistically . Five minutes Apgar score also showed same results i.e., lowest in zone I (5.6±1.5) and with higher results in Zone III (6.64±2.5). The oxygen therapy was given for longest duration in patients in zone II (30.7±3.4days) and Zone III patients received it for shortest duration (10.5±1.1) which was statistically significant.

Thomas K. et al. studied more than 9000 children and noted that 12.7% infants had severe disease. These infants had risk factors like small for gestational age, less gestational age, more blood transfusions, use of inotropes and delivery outside the hospital. Early Gestation, small and sick infants were at increased risk of severe disease[11].

Enomoto H at al. studied 143 infants having gestational age 32 weeks or less. Severe ROP was diagnosed when photocoagulation due to disease progressing to stage three was noted or they had 'plus disease'. The factors were evaluated between the severe and non-severe disease groups. Gestational age, birth weight, time period of oxygen supplement, period of positive air pressure and maximum fraction of inspiratory oxygen (FiO2) were related to severe disease in the univariate analyses. Longer duration of oxygen supplementation and high maximum FiO2 were significant risk factors associated with severe disease in multivariate analysis[12]. Khalesi N. in his study detects possible risk factors for retinopathy of prematurity (ROP), and a leading cause of childhood blindness treatable, among premature neonate. Parameters such as gestational age, birth weight, oxygen therapy, phototherapy etc. were collected and compared. It was found that lower gestational age, low mean first-minute Apgar scores, birth weight, phototherapy, and oxygen therapy were the factors affecting occurrence of ROP in premature infants. Higher birth weight and more advanced gestational age were protective factors for ROP. Oxygen therapy and multiple birth are risk factors of ROP and these can be used for prediction of ROP occurrence[13]. Results of our study are accordance the above mentioned studies.

5. Conclusion

The most common risk factors associated with development of ROP are gestational age, birth weight, First minute Apgar score, duration of oxygen therapy and the blood transfusion. Earliest gestation and low Apgar score was more associated with active ROP. Screening on time and interventions are important in preventing blindness and visual impairment in infants.

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