

An Assessment of the Risk Factors for Retinopathy of Prematurity in Preterm Very Low Birth Weight Babies

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Abstract

Introduction: Retinopathy of prematurity (ROP) is a vasoproliferative disorder of the retina among preterm infants which is the main cause of blindness in premature infants but recognized as leading cause of preventable blindness and visual impairment in children if treated early. It is a multifactorial disease in which retinal blood vessels of premature preschoolers fail to grow and develop normally, resulting in visual impairment and blindness. **Objectives:** The objective of the study is to assess the risk factors for retinopathy of prematurity in preterm very low birth weight babies. **Material & Methods:** This was a prospective observational study conducted at Special Care Baby Unit (SCABU), Department of Neonatology and Pediatrics, Department of Ophthalmology; Bangladesh Institute of Research and Rehabilitation for Diabetes, Endocrine and Metabolic Disorders (BIRDEM) from October 2016 to March 2017. One hundred and twenty-nine (129) preterm very low birth weight infants admitted in SCABU, BIRDEM during the study period were selected considering the inclusion and exclusion criteria. Data were analyzed using SPSS version 20.0 and were expressed as mean \pm standard deviation. **Results:** All babies weighed less than 1500 gm, among them 11 (12.2%) were < 1000 gm and 79 (87.8 %) were \geq 1000-1500gm. Forty-three, 43(47.8%) baby's gestational age was \leq 32 weeks and forty-seven 47(52.2%) baby's gestational age was >32 weeks, 74(82.2%) were inborn, 16 (17.8%) were out born. Seventy-nine, 79 (87.8%) were delivered by LUCS and 11(12.2%) by NVD. **Conclusion:** This study concluded that overall frequency of ROP was 30% among screened infants. Among the ROP diagnosed cases 11.1% required anti VEGF injection, 14.8 % received laser therapy. Lower gestational age, use of mechanical ventilator and frequent blood transfusions were found to be the most significant risk factors. There are few studies on the incidence and risk factors of this important morbidity in the developing countries. Taking known preventive measures, early detection and management of ROP can prevent blindness. The prognosis for maintaining functional vision is poor in advanced cases of ROP even with the application of currently available methods of treatment.

Keywords: Retinopathy of prematurity, Low Birth Weight, Preterm, Pediatrics.

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I. INTRODUCTION

Retinopathy of prematurity (ROP); initially known as retrolental fibroplasia coined by Terry in 1942 as a condition associated with premature babies [1]. It is a vasoproliferative disorder of the retina among preterm infants which is the main cause of blindness in premature infants but recognized as leading cause of preventable blindness and visual impairment in children

if treated early [2-4]. It is a multifactorial disease in which retinal blood vessels of premature preschoolers fail to grow and develop normally, resulting in visual impairment and blindness [5]. A baby developing blindness in early days of life can never regain vision and will have no perception of light of the colorful world, he or she has to bear this lifetime visual disability as a long-lasting scar of premature birth [6].

The key pathological change in ROP is peripheral retinal neovascularization [7]. Normal retinal vascularization progresses in utero from the disc margin (16 weeks) and reaches the nasal ora serrata (by 36 weeks) and then temporally (by 39-41 weeks) to complete a mature vascular retina [8, 9]. In premature or low birth weight infants treated with oxygen, immature retinal vessels in temporal retinal periphery constrict and ischemia developed. Retinal ischemia may result in up-regulation of proangiogenic factors such as Vascular Endothelial Growth Factor (VEGF) and lead to retinal angiogenesis. Subsequent contraction of the resulting peripheral retinal neovascular membrane may drag the temporal aspect of the retina toward the posterior pole, later may cause retinal detachment⁹. Other putative risk factors include asphyxia, mechanical ventilation, sepsis, intraventricular haemorrhage, respiratory distress, surfactant therapy, anemia, frequent blood transfusions, apnoea, hyperbilirubinemia, multiple gestation, delay in regaining birth weight [3, 5, 8, 10-18]. Term infants have completely vascularized retina and hence are not at risk for developing ROP. Preventive measurements are the best treatment, if disease occurs; it should be followed up very closely¹⁹. ROP may resolve without treatment by itself or can cause complications such as moderate to severe visual impairment like strabismus, amblyopia, cataract etc [20, 21].

II. OBJECTIVES

a) General objective:

- To find out the risk factors for retinopathy of prematurity in preterm very low birth weight babies.

b) Specific Objectives:

- To identify and afford appropriate treatment in the babies who have already established ROP
- To identify the Multivariant logistic regression of the factors and association of ROP
- To identify the risk factors which influence to ROP in preterm very low birth weight babies.

III. METHODOLOGY AND MATERIALS

This was a prospective observational study conducted at Special Care Baby Unit (SCABU), Department of Neonatology and Pediatrics, Department of Ophthalmology; Bangladesh Institute of Research and Rehabilitation for Diabetes, Endocrine and Metabolic Disorders (BIRDEM) from October 2016 to March 2017. One hundred and twenty-nine (129) preterm very low birth weight infants admitted in SCABU, BIRDEM during the study period were selected considering the inclusion and exclusion criteria. Data were collected in pre-formed questionnaire. Infants and mothers' demographic

information were collected from the parents. Clinical variables were collected during the hospital stay. Indirect ophthalmoscopy was done in SCABU on the scheduled day if the baby was still admitted. Before enrollment in the study, parents were informed about ROP, purpose, procedure of ROP screening, benefit and risk of the procedure by oral communication and written consents were taken from them. Data analysis was performed by using SPSS version 20.0. Data were expressed as mean \pm standard deviation. P-values \leq 0.05 (at 95% CI) were considered statistically significant.

Inclusion Criteria

- All newborn babies with a gestational age of 35 weeks or less at birth and a birth weight of 1500gm or less admitted at SCABU in BIRDEM General Hospital

Exclusion Criteria

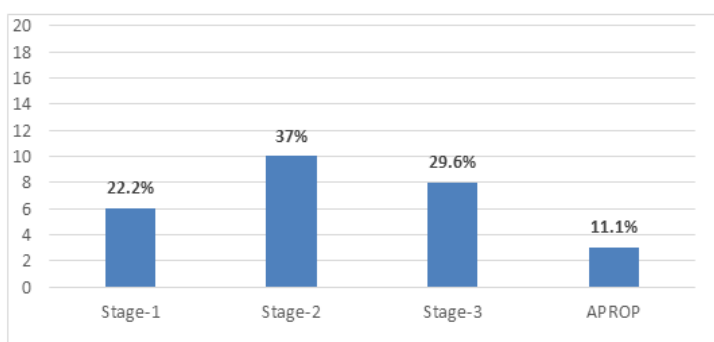
- Newborns who died before the first ophthalmologic inspection
- Newborns suffering from multiple and/or fatal hereditary incongruities
- Parents who did not give consent

IV. RESULTS

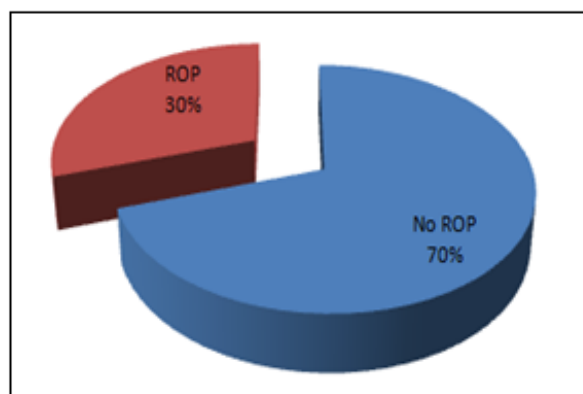
Among the study population 41(45.6%) were male and 49 (54.4%) were female (Table 1). All babies weighed less than 1500 gm, among them 11 (12.2%) were < 1000 gm and 79 (87.8 %) were \geq 1000-1500gm. Forty-three, 43(47.8%) baby's gestational age was \leq 32 weeks and forty-seven 47(52.2%) baby's gestational age was >32 weeks, 74(82.2%) were inborn, 16 (17.8%) were out born. Seventy-nine, 79 (87.8%) were delivered by LUCS and 11(12.2%) by NVD. Fifty three percent, 53.3% (47) mothers were in age group less than 29 years; twenty-eight, 31.1% (28) mother suffered from DM, 44.4% (40) mother had hypertension, 7.8% (7) suffered from APH and 33.34% (33) mother had PROM for more than 18 hrs. None of these five factors were significantly associated with ROP (Table 3). These factors (Gestational age, Frequent blood transfusion, IMV was significantly associated with ROP, P value < 0.05 (Table 4). Stepwise logistic regression analysis among all factors (revealed at univariant analysis) showed (Table 5) only lower gestational age [OR=0.201, 95% CI (0.068-0.596), P=0.004], frequent blood transfusion [OR=0.103, 95% CI (0.012-0.901), P=0.040] and use of mechanical ventilator [OR=0.241, 95% CI (0.051-1.144), P=0.041] significantly associated with occurrence of ROP. Among all diagnosed ROP neonates are follow up regularly and eleven percent, 11.1% (03) cases received anti VGEF injection and fourteen percent, 14.8% (04) received laser therapy (Table 6).

Table 1: Baseline characteristics of the study neonates (N=90)

Parameters	Frequency (n)	Percentage (%)
Sex		
Male	41	45.6
Female	49	54.4
Birth weight (gm)		
< 1000	11	12.2
≥1000-1500	79	87.8
Gestational age (weeks)		
≤32	43	47.8
>32	47	52.2
Place of delivery		
Inborn	74	82.2
Outborn	16	17.8
Mode of delivery		
LUCS	79	87.8
NVD	11	12.2

**Figure 1: Stages of ROP among studied infants (n=27). Out of 27 infants, 22.2% (6) had stage 1, 37% (10) at stage 2, 29.6% (8) at stage 3 and 11.1% (3) infants had APROP****Table 2: Frequency of ROP of the study neonates (N=90)**

Parameters	Frequency (n)	Percentage (%)
ROP	27	30.0
No ROP	63	70.0
Staging of ROP		
Stage- I	6	22.2
Stage- II	10	37.0
Stage-III	8	29.6
AP-ROP	3	11.1

**Figure 2: Pie chart of frequency of ROP among the study neonates**

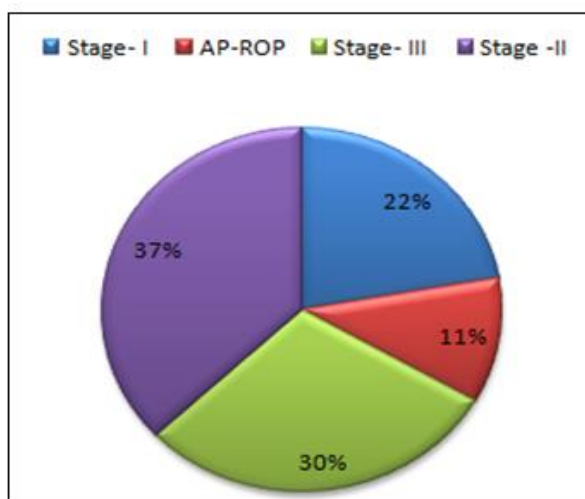


Figure 2: Pie chart of different stages of ROP among studied infants

Table 3: Distribution of maternal factors and association of ROP (N=90)

Parameters	ROP		OR (95% CI)	P value
	Positive (n=27)	Negative (n=63)		
Age				
≤29	12 (44.4%)	35 (55.6%)	0.64 (0.25-1.58)	0.334
>29	15 (55.6%)	28 (44.4%)		
DM				
Yes	7 (25.9%)	21 (33.3%)	0.70 (0.25-1.91)	0.487
No	20 (74.1%)	42 (66.7%)		
HTN				
Yes	11 (40.7%)	29 (46.0%)	0.80 (0.32-2.01)	0.643
No	16 (59.3%)	34 (54.0%)		
APH				
Yes	3 (11.1%)	4 (6.3%)	1.84 (0.38-8.86)	0.424
No	24 (88.9%)	59 (93.7%)		
PROM				
Yes	12 (44.4%)	18 (28.6%)	2.00 (0.78-5.09)	0.143
No	15 (55.6%)	45 (71.4%)		

Table 4: Distribution of neonate with different factors and association of ROP (N=90)

Parameters	ROP		OR (95% CI)	P value
	Positive (n=27)	Negative (n=63)		
Sex				
Male	12 (44.4%)	29 (46.0%)	0.93 (0.37-2.32)	0.890
Female	15 (55.6%)	34 (54.0%)		
Birth weight (gm)				
< 1000	5 (18.5%)	6 (9.5%)	2.15 (0.59-7.80)	0.233
≥ 1000- 1500	22 (81.5%)	57 (90.5%)		
Gestational age (weeks)				
≤32	19 (70.4%)	24 (38.1%)	3.85 (1.46-10.18)	0.019
>32	8 (29.6%)	39 (61.9%)		
BT				
Yes	26 (96.3%)	47 (74.6%)	8.85 (1.11-70.58)	0.018
No	1 (3.7%)	16 (25.4%)		
Oxygen use				
Yes	23 (85.2%)	49 (77.8%)	1.64 (0.48-5.54)	0.421
No	4 (14.8%)	14 (22.2%)		
CPAP				
Yes	14 (51.9%)	21 (33.3%)	2.15 (0.85-5.39)	0.099
No	13 (48.1%)	42 (66.7%)		
IMV				
Yes	7 (25.9%)	3 (4.8%)	7.00 (1.65-29.66)	0.007
No	20 (74.1%)	60 (95.2%)		

Table 5: Multivariate logistic regression of the factors and association of ROP (N=90)

Anomalies	B	Wald	p value	OR	95% CI (min-max)	
Gestational Age (≤ 32)	-1.603	8.373	0.004	0.201	0.068	0.596
Blood Transfusions (Yes)	-2.271	4.220	0.040	0.103	0.012	0.901
Intermittent Mode of Ventilation (IMV) (Positive)	-1.424	3.207	0.041	0.241	0.051	1.144
Intraventricular Hemorrhage (IVH) (Positive)	-0.906	2.403	0.121	0.404	0.128	1.271

Table 6: Treatment received of neonates having ROP (N=27)

Treatment Option	Frequency (n)	Percentage (%)
Avastin (anti VGEF)	03	11.1
laser therapy	04	14.8
No Treatment	20	74.07

V. DISCUSSION

It has also been well documented that very low birth weight babies may develop early and aggressive posterior ROP (AP-ROP)⁸. The rapidly progressive type of ROP that can lead to retinal detachment without treatment³⁶. Current screening criteria in the United States and many developed countries are based on gestational age (GA) and weight at delivery [22-25]. In our study, the hospital prevalence of retinopathy of prematurity was 30% among premature very low birth weight infants. Another study of Bangladesh showed, 35% of the screened infants had ROP [26]. From Different studies conducted at India, the incidence of ROP was reported in between 24 and 47% among high risk preterm infant populations [27, 28]. Incidence of ROP in developed countries is estimated to be 10-27% depending on degree of prematurity and birth weight [29]. The frequency is similar with that of studies conducted in developed and developing countries [12]. There are few studies on the incidence and risk factors of this important morbidity in the developing countries. Taking known preventive measures, early detection and management of ROP can prevent blindness. The prognosis for maintaining functional vision is poor in advanced cases of ROP even with the application of currently available methods of treatment. Preterm infants are at a much higher risk for ROP which can be prevented by addressing potential modifiable risk factors and strengthen screening protocol for detection of ROP at an early stage [6, 10]. From this study it has been known that a significant number of infants (18.5% of ELBW and 81.5% of VLBW infants) have the disease, but actual situation could not be effectively estimated due to large number (10.07%) of drop out and small sample size. In this study association between maternal perinatal factors and the development of ROP was looked for. Maternal hypertension, DM, APH, PROM and mode of delivery had no significant association with occurrence of ROP (P values were 0.643, 0.487, 0.424 and 0.143 respectively). One study showed that vaginal delivery was a significant and independent predictor of severe ROP. There was no difference in the occurrence of ROP and mode of delivery in our study. There was no significant difference in occurrence of ROP between the singleton and multiple gestation groups. In our study 6 (70%) out

of 10 (11.1%) neonates who got mechanical ventilation developed ROP, which is statistically significant (P value=0.007). Some other studies have got the similar result.

VI. LIMITATIONS OF THE STUDY

1. Sample size was small.
2. Short duration of study period.
3. As a single centered study, the results may not be applicable for all infants.
4. Drop out of some babies could not be avoided.

VII. CONCLUSION AND RECOMMENDATIONS

This study determined that out of several significant risk factors, lower gestational age, use of mechanical ventilator and frequent blood transfusions were found to be the most significant risk factors. Our study demonstrated the increased frequency of ROP in very low-birth weight babies. Studies with larger sample size should be undertaken to find out the real representation of ROP and associated risk factors among the preterm very low birth weight newborns of our country. To control blindness due to ROP there is an urgent need to increase awareness among the public, health professionals and parents. Therefore, it is critical to adopt better care for disease prevention, timely screening, and appropriate treatment programs for the neonates who are at the risk of this disease.

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