Original Article

Frequency and Risk Factors for Retinopathy of Prematurity in Very Low Birth Weight Infants in NICU, BSMMU

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Abstract

Introduction: Retinopathy of prematurity (ROP) is emerging as an important avoidable cause of childhood blindness both in developed and developing countries that primarily affects premature and very low birth weight infants. There has been paucity of studies on this topic in Bangladesh and there is no national prevalence data on ROP to understand the real burden of the disease. Hence this study has been undertaken to see its frequency and risk factors for ROP in very low weight infants admitted in NICU, BSMMU.

Objectives: To find out the frequency and risk factors for ROP in very low birth weight infants admitted in NICU, BSMMU.

Methodology: It was a prospective observational study and was carried out in the Department of Neonatology and Department of Ophthalmology, BSMMU from January 2014 to June 2015. Considering all inclusion and exclusion criteria total 162 very low birth weight neonates were enrolled in the study. ROP screening was performed as per unit protocol. All eye examinations were undertaken by experienced ophthalmologist who was especially trained in ROP.

Result: Out of 162 study population, one hundred forty fore (88.9%) were very low birth weight, 18(11.1%) were extremely low birth weight and mean birth weight was 1294.35 (SD: 180.96) g.

Frequency of ROP was 38(23.5%), where 30(20.83%) among very low birth weight (VLBW) and 8(44.44%) were among ELBW neonates. Out of 38 ROP cases, 5(13%) had stage 1 retinopathy, 3(8%) had stage 2 retinopathy, 16(42.1%) had stage 3 and remaining 14(36.8%) neonates had APROP. On univariate analysis seventeen factors were found to be significant but on stepwise logistic regression analysis only lower gestational age [OR=5.014; CI(95%),2.160-11.640, P=.001] and use of mechanical ventilator [OR=1.925; CI(95%),1.133-3.269, P=.015] was found to be the most significant for causation of ROP.

Conclusion: The overall frequency of ROP was 38(23.5%), where as 30(20.83%) were among VLBW and 8(44.44%) were among ELBW neonates. Prevention of prematurity and judicious use of ventilator may reduce the incidence and severity of ROP

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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.[1] It is a multi factorial disease in which retinal blood vessels of premature infants fail to grow and develop normally, resulting in visual impairment and blindness.[2] Term infants have completely vascularized retina and hence are not at risk for developing ROP.

The incidence of ROP in different regions of the world vary from 7 to 37%.[3] In developed countries it is 10–27% depending on degree of prematurity and birth weight.[4] Studies from India have reported ROP in 20% to 52% of screened neonates. More recent studies reporting lower rates of ROP ranging from 20% to 30%.[5] Though there is no national prevalence data on ROP in Bangladesh, an investigation showed 40% of screened neonates suffered from ROP.[6]

ROP has emerged as a problem in developing countries because of advancement in neonatology for which survival of premature and very low birth weight neonates have been increasing.[7] Although, the most important risk factor for ROP is prematurity, several recent studies have suggested a multi factorial basis for ROP development. These are very low birth weight, oxygen therapy, prolonged mechanical ventilation, repeated blood transfusion, sepsis and prolonged parenteral nutrition.[8]

Preventive measures are the best treatment. If disease occurs it should be followed up very closely. Timing is one of the important factors that make the treatment successful in ROP, because the disease can advance very quickly and delayed treatment often reduces the chances of success.[9] It is, therefore, essential that health professionals know whom and when to screen for ROP in preterm infants.

National Neonatal Forum (NNF) in India recommends, screening for ROP should be performed in all preterm neonates who are < 34 weeks gestation and / or < 1750 grams birth weight. Apart from these infants, those preterm infants between 34 to 36 [6,7] weeks gestational age or a birth weight between 1750 and 2000 grams with risk factors for ROP should also be screened.[10,11] National guide line for ROP screening in Bangladesh is yet to be established, so unit protocol for screening in NICU, BSMMU was followed in the study

In Bangladesh there is no national prevalence data on ROP to understand the burden of disease. This study aimed to see the frequency of ROP and identification of risk factors among very low birth weight newborns admitted in NICU, BSMMU.

Materials and Methods

This prospective observational study was conducted at Department of Neonatology and Department of Ophthalmology of Bangabandhu Sheikh Mujib Medical University (BSMMU), Shahbagh, Dhaka. All candidates for ROP screening were examined in NICU routinely and subsequent follow up examination were performed in the Ophthalmology Department. Study period was from January 2014 to June 2015 and study population was very low birth weight (VLBW) neonates admitted in NICU, BSMMU, during the study period. Exclusion criterias were newborns with fatal congenital anomalies, congenital eye problems like cataract, glaucoma, corneal opacities etc The sample size was determined 189, considering: p = 40% , q = (100-40)% = 60%, d(precision) = .07 and z =1.96 at 95% confidence level.

Parents or attendants of the neonate who had fulfilled the inclusion criteria were informed about ROP. Purpose, procedure of screening, importance and benefit of the study were explained and written consent was taken from them before enrollment in the study. ROP screening was performed as per unit protocol. Infants whose birth weight less than 1200 gram were screened (First time) at 20 days of age and who had 1200 gram or more were screened at 30 days of age.

The examination was performed using a binocular indirect ophthalmoscope and 20 D lenses by experienced ophthalmologist who was especially trained in ROP. Staging of retinopathy was based on International Classification of ROP (ICROP).

Follow up examinations were done according to the advice of the ophthalmologist depending on the clinical condition of retina and grade of ROP. Reminder was given over telephone for confirmation the follow up visit. In severe ROP (Grade 3, 4) the eyes were examined every week and in mild ROP (Grade 1, 2) every 2-4 weeks until the resolution of ROP. ROP screening were terminated once there was complete vascularization of immature retina, or if the ROP had shown regression.

Data analysis:
Data management and analysis were performed by using SPSS version 20.0. During univariate analysis the categorical variables were tested with Chi square and Fisher exact test and for continuous variables Student's t-test. Multivariate logistic regression analysis was performed with the variables which were found significant by univariate analysis. P-values less than 0.05(at 95% CI) were considered statistically significant.

Ethical consideration
Ethical clearance was obtained from Institutional Review Board (IRB) of BSMMU to undertake the current study. According to Helsinki Declaration for Medical Research involving Human Subjects 1964, legal guardians of the newborn were informed and explained about the nature of study and they also informed about the right of the participants to withdraw themselves from the research at any time, for any reason. Written consent was taken from them if they voluntarily provided consent to participate in this study.

Limitations of the study
It was a single centered study, so it may not generalize the results to the whole infants and dropout rate was high, so some cases might be missed.

Results
During the study period, 189 cases of very low birth weight (VLBW) neonates were registered; out of them 6 cases died before the first ophthalmologic examination, 21 did not come back after discharge and remaining 162 cases were evaluated. So, ultimate sample size consisted of 162 neonates. The overall frequency of ROP was 38(23.5%), where 30(20.83%) were among VLBW and 8(44.44%) were among ELBW neonates.
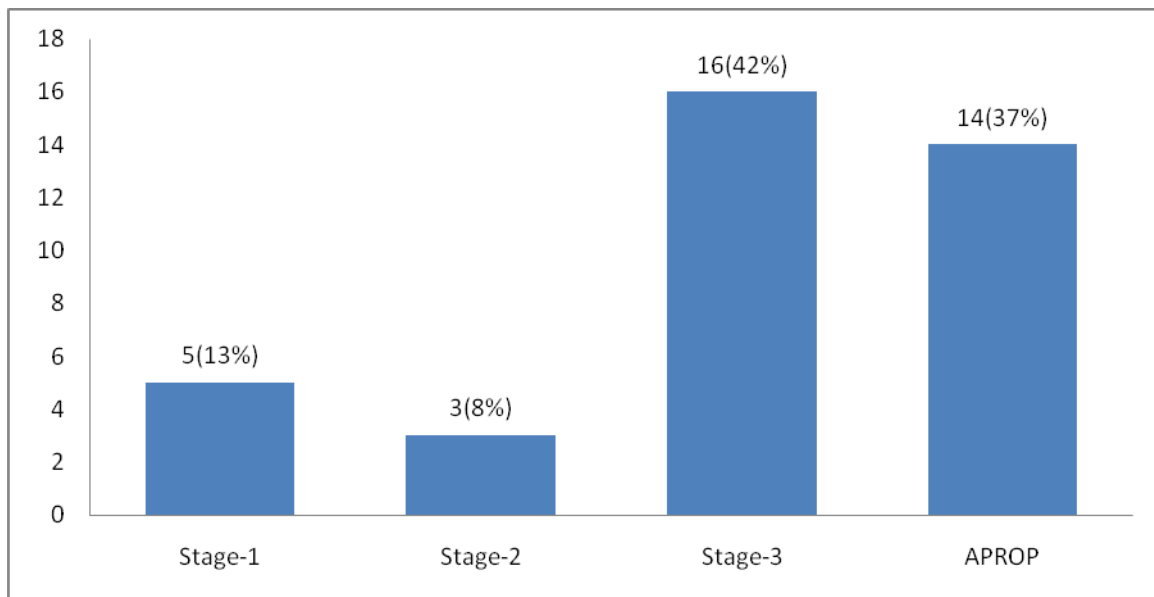
Table 1: Base line characteristics of the study neonates (N=162)

Parameters		Number	Percentage
Sex	Male	96	59
	Female	66	41
B.Wt	<1500g	144	89
	<1000g	18	11
G.Age	<28 wks	2	1.5
	28-31 wks	68	42
	>31 wks	92	56.5
Inborn		120	74
Outborn		42	26
Mode of delivery	LUCS	123	76
	NVD	39	24

Among the study population 96(59%) were male and 66(41%) were female. Considering birth weight 144(89%) belong to VLBW and 18(11%) ELBW. Sixty eight (42%) were very preterm, 92(56.5%) were

mild preterm, 2(1.5%) were extremely preterm. 120(74%) were inborn, 42(26%) were outborn. 123(76%) were delivered by LUCS and 39(24%) by NVD.

Figure 1 : Staging of ROP among studied neonates (n=38).

Out of 38cases, 5 (13%) diagnosed as stage 1 retinopathy, 3 (8%) stage 2 retinopathy, 16(42.1%) stage 3 and 14(36.8%) neonates as APROP.

Tab 2: Birth weight and association of ROP.

B.wt	ROP		ODDs ratio(95% CI)	P value
	Yes	No		
<1500g	30(21%)	114(79%)	3.040(1.104-8.371)	.037
<1000g	8(44%)	10(56%)		
Total	38	124		

Frequency of ROP in ELBW infants was 44% and in VLBW neonates that was 21%. Frequency of ROP was inversely proportional to birth weight and it was statistically significant [OR=3.040; 95% CI(1.104-8.371), P=.037].

Tab 3: Distribution by gestational age and association of ROP

G. age	ROP		Odds ratio(95%CI)	P value
	Yes	No		
<32wks	29(41%)	41(59%)	6.52(2.827-15.053)	.001
≥32 wks	9(10%)	83(90%)		
Total	38	124		

The frequency of ROP according to gestational age. As the gestational age decreased, the incidence of ROP increased which was statistically significant [OR=6.52; 95% CI (2.827-15.053), P=.001].

Tab 4: Ventilator use and association of ROP.

Ventilator	ROP		ODDs ratio(95% CI)	P value
	Yes	**No**		
Yes	10(59%)	7 (41%)	5.969[2.088-17.062]	.001
No	28(19%)	117(81%)		
Total	38	124		

Ventilator use was significantly associated with ROP occurrence [OR=5.969; 95% CI(2.088-17.062), P=.001].

Tab 5: Step wise Logistic Regression Analysis.

Variables	Exp(B)	95% C.I for Exp(B)		P-value
		Lower limit	Upper limit	
Sex	1.832	.749	4.483	.185
PNA	1.432	.571	3.591	.443
Sepsis	1.269	.489	3.297	.624
RDS	1.461	.562	3.566	.461
Ventilator support	1.925	1.133	3.269	.015*
Gestational age	5.014	2.160	11.640	.001*
Anemia	1.485	.536	4.114	.447
Pneumonia	1.102	.33	3.952	.872
Apnea	1.046	.334	3.272	.939
Birth weightt	1.492	.179	.517	.222
HTN	3.305	.775	1.601	.203
CLD	1.545	.140	.465	.211
APH	4.534	.633	1.694	.294
Meningitis	3.154	.211	.816	.768
Sepsis	3.400	.495	1.297	.596
Pneumonia	3.592	.338	1.102	.872
B.Transfusion	3.057	.299	.956	.939

The above table showing stepwise logistic regression analysis with seventeen factors which were found significant on univariate analysis.

On univariate analysis seventeen factors found to be significant. Those were maternal pre eclampsia and antipartum hemorrhage, male sex, lower birth weight, prematurity, perinatal asphyxia, apnea, anemia, blood transfusion, sepsis, meningitis, pneumonia, respiratory distress syndrome, chronic liver disease, oxygen therapy, use of CPAP and mechanical ventilator. Stepwise logistic regression analysis was done

including all these seventeen factors and finally lower gestational age [OR=5.014; CI(95%),2.160-11.640, P=.001] and use of mechanical ventilator [OR=1.925; CI(95%),1.133-3.269, P=.015] was found to be most significant for causation of ROP.

Discussion

Retinopathy of prematurity (ROP) has been acknowledged as one of the major causes of blindness in infants and children in developed countries, and has emerged as a problem in developing countries as well. This is because of advancement in neonatology for which survival of premature and very low birth weight neonates have been increasing in the developing countries.[7,12] ROP is an important cause of potentially preventable blindness in developed countries.[13,14] In developing countries it is emerging as an epidemic.[15]

During this study period large number of the parents failed to come for ROP screening. Total drop out was 24(15%). The failure to attend to the ophthalmologist was probably due to the parent's fatigability after a long stormy hospital stay or due to long distance of the residence and financial constraints. Lack of awareness among parents as well as family physicians regarding ROP was also an important cause.

In this study, the overall frequency of retinopathy of prematurity was 23.5% where 20.83% were among VLBW and 44.44% were among ELBW neonates. The finding was found to be similar in the studies conducted in developing countries like India where incidence of ROP has been reported at 24% - 47% among high risk preterm infants.[16, 17].

A good number of studies have proven the relationship between very low birth weight and occurrence of ROP.[13,16,18,19] Our study demonstrated the increased frequency of ROP in very low-birth weight babies which is comparable to most studies.

This study showed significant association of male sex with occurrence of ROP. Some studies also found the same.[20] Blood transfusion showed no significant association with ROP but tend to be significant (p value .05). But some studies found significant association.[3,10,25]

Mechanical ventilation had a strong association with the occurrence of ROP. In this study we had 17(10%) neonates who got mechanical ventilation support and 10(59%) of them developed ROP, and it was statistically significant (P=.001). Some other studies have got the similar result.[2,19,22,23,24]

This study also showed perinatal asphyxia, meningitis, pneumonia, respiratory distress syndrome, chronic lung disease, apnea and use of CPAP had significant association with occurrence of retinopathy of prematurity (ROP), where P values were .039, .029, .035, .031, .011, .016, .005 respectively. Findings are similar with the findings of most of the studies investigating risk factors of ROP.[2,23]

Total seventeen significant factors were found to be related with occurrence of ROP on univariate analysis. Later, stepwise logistic regression analysis was done including all of these factors. Finally lower gestational age and use of mechanical ventilator was found to be most significant. P values were .015 and .001 respectively.

From this study it has been known that a significant number of neonates (20.83% of VLBW and 44.44% of ELBW neonates) have the disease, but actual situation could not be effectively estimated due to huge drop out and small sample size. So, studies in larger scale should be undertaken to know the exact frequency and risk factors in our set up.

Conclusion

The overall frequency of ROP was 38(23.5%), where as 30(20.83%) were among VLBW and 8(44.44%) were among ELBW infants. Seventeen risk factors were significantly associated with ROP, among them lower gestational age and use of mechanical ventilator had strong association. Prevention of prematurity and judicious use of ventilator may reduce the incidence and severity of ROP.

Recommendations:

Studies in larger scale (multi centre study) with larger sample size should be undertaken to find out the real picture 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.

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