

ORIGINAL ARTICLE

CHARACTERISTICS OF PRETERM WITH SIGHT THREATENING
RETINOPATHY OF PREMATURITY

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Background: Retinopathy of prematurity (ROP) is a preventable and treatable vaso-proliferative disorder of the retina which develops mostly in preterm babies. It is a leading cause of childhood blindness and more common in under developed countries. Prevalence of the severe ROP is 7.7% in Pakistan. We reviewed the characteristics of preterm babies with severe ROP to evaluate the predictors of sight threatening ROP. **Methods:** Our study was conducted at the NICU of Aga Khan University Hospital which is a tertiary care private sector hospital in Karachi. Ninety-seven cases of severe ROP were found out of which 83 cases were enrolled. Data on determinants for ROP were collected including gestational age, birth weight, weight gain at two and four weeks, h/o blood transfusion, supplementary oxygen, presence of PDA and its treatment. Data analysis was done by using SPSS version 20.0 **Results:** Frequency of severe ROP in our cohort was 5.95%. Mean gestational age for severe ROP was 28.27 ± 1.79 and mean birth weight was 1069.16 ± 271.71 grams. The overall mean weight gain per week in these babies was 94.62 ± 75.64 grams. Supplementary oxygen was provided in almost 100% (82/83 cases) of cases. Surfactant was given to 56.6 % babies. PDA was found in 23 cases out of which 19 were treated by medical therapy whereas surgical treatment was done in 4 cases. **Conclusion:** Severe Retinopathy of prematurity was directly correlated with low birth weight, and gestational age. An average, weight gain in four weeks was lower in ROP babies (94.62 ± 75.64 grams) than the recommended weight gain (WHO recommended 140–210 gm per week). This could be associated with the development and severity of ROP requiring treatment. Therefore, a prospective case control study is required to further identify risk factors associated with the above cohort. Screening and follow up of all such babies according to the international criteria is the need of the day.

Keywords: Child health; Retinopathy of prematurity; Low birth weight; Gestational age; Childhood blindness; Risk factors; Weight gain

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INTRODUCTION

Retinopathy of prematurity (ROP) is a preventable and treatable vaso-proliferative disorder of the retina which is mostly developed in preterm babies.^{1,2} In developed countries, severe ROP is less due to better screening and treatment facilities as compared to developing and under developed countries especially in Asia and Africa.³ The World Health Organization (WHO) has notified ROP as major cause of blindness in childhood in middle income group countries. ROP is becoming a public health problem in developing countries, because of huge number of preterm births along with improving NICU facilities.⁴

The most important risk factor for developing ROP is prematurity. More than 50 separate risk factors have been identified. In multivariate analysis, low birth weight, low

gestational age, assisted ventilation for longer than one week, surfactant therapy, high blood transfusion volume, cumulative illness severity, hyperglycaemia, and insulin therapy, have been independently associated with higher rates of ROP. Other possible risk factors include sepsis, fluctuations in blood gas measurements, intraventricular haemorrhage, bronchopulmonary dysplasia, systemic fungal infection, and early administration of erythropoietin for the treatment of anaemia of prematurity. However, three factors have shown consistent and significant association with ROP: low gestational age, low birth weight and prolonged exposure to supplementary oxygen following delivery.⁵ In Canada, United States, and United Kingdom, in severe ROP babies, mean birth weight was around 750 gm, with gestational age of 25 weeks.⁶

According to ICROP, there are five stages of the retinopathy of prematurity determined on the basis of ophthalmoscope assessment: stage 1 is a faint demarcation line, stage 2 is an elevated ridge, stage 3 is an extra retinal fibro vascular tissue, and stage 4 is a subtotal retinal detachment, while stage 5 is a total retinal detachment.⁷ While Plus disease indicates significant vascular dilation and tortuosity which may be present at any stage and indicate the increased blood flow through the retina.⁷ The survival rate of premature babies has improved due to current advancement in the neonatal care. It can be related to simultaneous increase in the ROP cases worldwide.⁷

Some factors responsible for ROP in our part of the world differ from the developed countries owing to the limited resources and an overall deficiency of quality and standards of healthcare at all levels nationwide. Some of these include unavailability of standard screening protocols and treatment programs, substandard neonatal care, lack of awareness in paediatricians and neonatologist to recognize and treat complications of preterm births including ROP and unavailability of high standard NICU facilities.^{8,9}

In a study done in India¹⁰, it was noted that majority (86.4%) of babies suffering with stage 5 of ROP were not screened at all. Another study from India¹¹ suggests that where no ophthalmologist is available, even tele-screening by a non-ophthalmologist reduces the incidences of severe ROP. With the increasing incidence rates of ROP in developing countries like Pakistan, where international screening program are not followed, it is imperative to review local literature so that importance of ROP screening is emphasized all over the country for paediatricians and others concerned.

MATERIAL AND METHODS

This retrospective cohort study was conducted at the NICU of Aga Khan University Hospital which is a tertiary care private sector hospital in the largest city of Pakistan. It is a level 3 unit with 24 beds and serves as a referral centre for all multidisciplinary neonatal medical and surgical care. Retrospective data was collected by chart reviews for all babies admitted with severe ROP for laser/surgical procedures in NICU from 2002–2015. In our study we use the term “Severe ROP” for babies who were classified as having sight threatening ROP as per ICROP classification of that time requiring retinal ablative therapy. According to ICROP Retinal ablative therapy is

indicated for eyes with threshold retinopathy of prematurity (ROP) and eyes with high-risk pre-threshold retinopathy of prematurity (ROP) based on clinical findings.

During the study period, out of 1630 babies admitted in our unit who were at risk of developing ROP, 97 cases qualified for the criteria of severe ROP however 14 were excluded due to unavailability of data rest of the 83 cases were enrolled using a standardized pre-formed *Proforma*. The information regarding gestational age, weight of the baby at birth, at two and four weeks were taken into accounts along with blood transfusion history supplementary oxygen history, PDA treatment and other co-morbidities.

RESULTS

Frequency of severe ROP in our cohort was 5.95%. On the basis of selection criteria, overall 83 cases of Severe ROP were detected out of which 29 cases in 9 years from 2002–2010, and 54 cases in 5 years from 2011 to 2015 were detected showing a rising trend. (Figure-1)

According to data analysis, mean age of the mothers of a ROP child was 29.87 ± 4.82 years in which majority (68.7%) were between the ages of 25–35 years. Similarly, mean gestational age of babies with severe ROP was 28.27 ± 1.79 whereas majority (51.8%) of them were between 25–28 weeks of gestation. Mean weight of babies was 1069.16 ± 271.71 grams, majority (56.6%) of them were between 1000–1500 grams. The overall mean weight gain per week was found to be 94.62 ± 75.64 grams. (Table-1 and Figure-2)

Amongst the study population 86.7% received, antenatal steroids, whereas post-natal steroid was provided to only 16.9% cases. Supplemental oxygen was provided in almost all (82 of 83) cases and majority of them received it for 7–28 days. Surfactant was given to 56.6% babies. Patent ductus arteriosus was found in 23 cases out of which 19 were treated by medical therapy whereas surgical treatment was given to 4 cases. (Table-2) Amongst those who were medically treated 47.82% babies were given ibuprofen, 34.78% babies Indomethacin, 17.39% babies received diuretics and 8.70% babies were managed with fluid restriction. 53% babies developed sepsis. Total parenteral nutrition was provided to 89.2% babies and phototherapy in 90.2% babies. Intraventricular haemorrhage was found in 24.1% babies along with anaemia in 83.1% babies. However, Hyperglycaemia was found in only 3.6% cases. Similarly, in 17 cases no blood transfusion was carried out whereas in 55 babies up to 200 ml blood was transfused as

compared to 11 cases in which more than 200 ml blood was transfused. (Table-3) Severe Retinopathy of prematurity was directly correlated with low birth weight, and gestational age. (Table-4 & Figure-3). Amongst babies between GA 24–28 weeks 74.4% had a poor average weight gain of <100 grams per week whereas 25.5% had weight gain of over 100grams.This is in contrast with babies between 29–32 weeks where around 40% has weight gain of >100 grams per week.

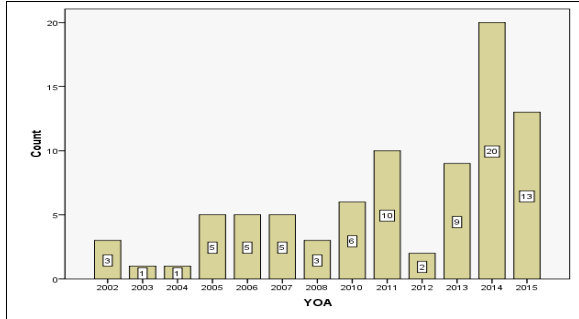


Figure-1: Frequency of ROP from 2002 - 2015

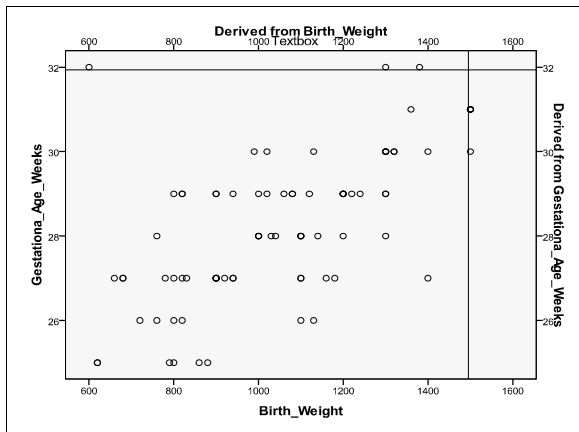


Figure-2 Birth weight in different Gestational ages.

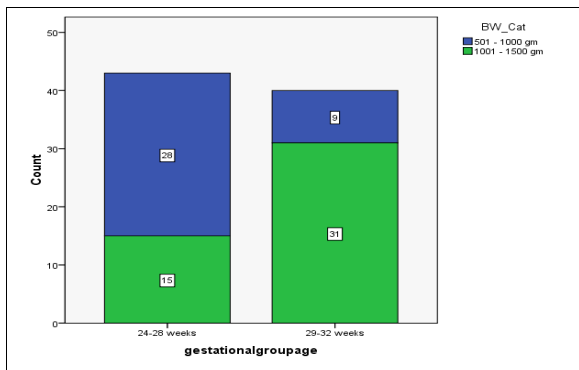


Figure-3 Distribution of severe ROP amongst different weight and gestation groups

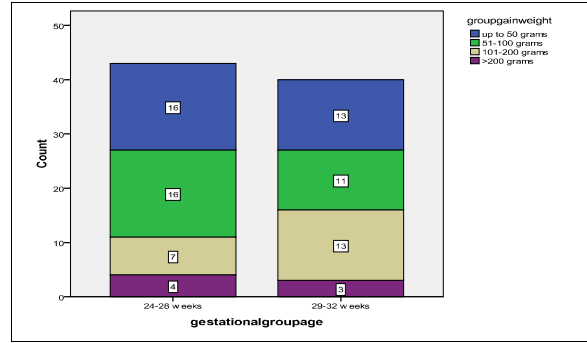


Figure-4: Weight Gain Distribution in different Gestational age groups

Table-1: Characteristics of mother and baby

Characteristics	Frequency	Percentage
*Mother Age (years)	29.87±4.82	
Up to 25 years	18	21.7
26–30 years	28	33.7
31-35 years	29	34.9
36 +	8	9.7
*Gestational Age (Weeks)	28.27±1.79	
24–28 weeks	43	51.8
29 weeks –32 weeks	40	48.2
Gender of baby		
Male	43	51.8
Female	40	48.2
*Baby weight (grams)	1069.16±271.71	
501–1000	36	43.4
1001–1500	47	56.6
*Total Weight at 2 weeks	1151.80±327.51	
*Weight gain at 2 weeks**	81.32±194.08	
*Total Weight at 4 weeks	1472.76±467.12	
*Weight Gain at 4 weeks**	404.32±327.41	
*Weight gain rate /week	94.62±75.64	

*Presented in Mean±SD. ** Difference between birth weight and after 4 weeks.

Table-2: Antenatal and postnatal treatment

Treatment	Frequency	Percentage
Antenatal Steroids		
Yes	72	86.7
No	11	13.3
Postnatal steroids		
Yes	14	16.9
No	69	83.1
Supplemental O₂		
Yes	82	98.8
No	1	1.2
O₂ Duration (82 cases)		
< 7 days	13	15.9
7 - < 14 Days	17	20.7
14 Days - <28 Days	27	32.9
>28 Days	25	30.5
Surfactant		
Yes	47	56.6
No	36	43.4
PDA		
Yes	23	27.7
No	60	72.3
PDA treatment		
Medical	19	82.6
Surgical	4	17.4

Table-3: Antenatal and postnatal treatment

	Frequency	Percentage
Med Ibuprofen		
Yes	11	47.82
No	12	52.17
Med Indomethacin		
Yes	8	34.78
No	15	65.21
Med Diuretics		
Yes	4	17.39
No	19	82.60
Med Fluid Restrict		
Yes	2	8.70
No	21	91.30
Sepsis		
Yes	44	53.0
No	39	47.0
TPN (Total parenteral nutrition)		
Yes	74	89.2
No	9	10.8
Phototherapy		
Yes	75	90.4
No	8	9.6
IVH (Intraventricular haemorrhage)		
Yes	20	24.1
No	63	75.9
Hyperglycaemia		
Yes	3	3.6
No	80	96.4
Anaemia		
Yes	69	83.1
No	14	16.9
Blood transfusion (66 cases)		
Up to 200	55	83.3
More than 200	11	16.7

Table- 4: Gestational age vs birth weight

	Gestational age	Birth weight			p value
		501-1000 grams	1001-1500 grams		
	24-28 weeks	28	15	43	0.000
	29-32 weeks	9	31	40	
	Total	37	46	83	

DISCUSSION

In the recent period, a high raising trend of severe retinopathy of prematurity (ROP) was observed. In our study, overall 83 cases of Severe ROP were detected in 14 years period, out of which 29 cases in 9 years from 2002-2010, whereas 54 cases in 5 years from 2011 to 2015, showing a rising trend.

According to a study¹³, a total of 301 infants were screened: 27 (9%) babies developed ROP, of which 19 had stage 3 ROP or worse. In another study⁷ Out of the studied 172 infants, 33 infants (19.2%) developed ROP in one or both eyes; 18 (54.5%) cases stage 1, 9 (27.3%) cases stage 2, and 6 (18.2%) cases stage 3. In a study conducted in Pakistan², 24.6%

developed retinopathy of prematurity. In our study only 5.95% babies developed severe ROP.

In a study⁵ conducted in Colorado, United State, the mean gestational age of participants was 28.8±2.5 weeks and mean birth weight of 1280.34±350.43 g. In another study^{5,13} mean gestational age was 29.6±1.9 and 29.8±1.9 weeks respectively. In the study¹³ mean birth weight was 1124±239.5 grams. In our study, the mean gestational age of the ROP babies were 28.27±1.79 weeks and mean weight of Severe ROP babies was 1069.16±271.71 grams, which is almost equal to the previous studies.

In a study² conducted in Lahore, Pakistan, supplement oxygen was provided to 58.6% babies. In another study⁶ almost all the babies were provided supplement oxygen. The mean duration of oxygen supplement was found 19.5 days. In our study supplement oxygen was also provided in almost all 82/83 cases and majority of them received it for 7 to 28 days. Surfactant was given to 56.6% babies.

Patent ductus arteriosus was found in 23 cases out of which 19 were treated by medical therapy whereas surgical treatment was given to 4 cases. According to medical treatment, 47.82% babies were given ibuprofen, 34.74% babies Indomethacin, 17.39% babies Diuretics and 8.70% babies were given fluid Restrict. No other study focused on this important parameter.

In a study², sepsis was found in only 8.8% cases, anaemia in 30.2% cases and blood transfusion in only 15.6% cases. In contrast to these, our study results showed sepsis in 53% babies, anaemia in 83.1% of the ROP babies.

In another study¹², only gestational age (adjusted relative risk 0.774, 95% CI 0.603 to 0.994) was independently associated with the development of ROP. According to a study conducted in Egypt⁷, significant relationship between the occurrence of ROP and gestational age ($p=0.000$), sepsis ($p=0.004$), oxygen therapy ($p=0.018$), and frequency of blood transfusions ($p=0.030$). In another study¹³ low birth weight by six weeks was found an independent risk factor of severe ROP. In our study Severe Retinopathy of prematurity was directly correlated with low birth weight, and gestational age. It was observed that out of 43 cases of gestational age 24-28 weeks, 32, i.e., 74.4%, the weight gain per week was just up to 100grams and only 11 babies, i.e., 25.5% gained weight for more than 100 grams per week on an average. Against this, 16 babies, i.e., 40% gain weight more than 100 grams whose mothers were deliver their babies in 29-32 weeks of their gestational age.

CONCLUSION

Retinopathy of prematurity (ROP) is a preventable disease of retina. Severe Retinopathy of prematurity

was directly correlated with low birth weight, and gestational age. An average, weight gain in four weeks was lower in ROP babies (94.62±75.64 grams) than the recommended weight gain (WHO recommended 140–210 gm per week). This could be associated with the development and severity of ROP requiring treatment. Therefore, a prospective case control study is required to further identify risk factors associated with the above cohort. Screening and follow up of all such babies according to the international criteria is the need of the day.

RECOMMENDATIONS

Proper screening of the preterm and low birth weight babies is the key factor to control the severe retinopathy of prematurity or blindness of childhood in the country. For this purpose, strict compliance of the AAPOS criteria is necessary. A larger study is needed to determine the proper prevalence of the sever ROP in the country.

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CONFLICT OF INTEREST

All authors disclose any financial and personal relationships with other people or organization that could inappropriately influence their work.

AUTHORS' CONTRIBUTION

SA: Conceptualization of study, final approval and review of manuscript. ASH: Study design, review, literature search. MH & AA: Data collection & study protocol writing. KA: Helped in protocol writing.

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