

Incidence of Retinopathy of Prematurity in Infants with Low Gestational Age and Low Birth Weight

Bilal Humayun Mirza¹, Kanwal Zareen Abbasi², Muhammad Rizwan Khan³, Munib Ur Rehman⁴, Maria Zubair⁵, Fuad Ahmad Khan Niazi⁵

Abstract:

Objectives: To determine the incidence of retinopathy of prematurity in infants with low gestational age and low birth weight.

Methods: An institution based cross-sectional study was conducted in the department of Ophthalmology, Holy Family Hospital, Rawalpindi in collaboration with department of Paediatrics, Holy Family Hospital for a duration of 12 months. Sample of 85 was collected using non probability consecutive sampling technique. 85 babies born before 34 weeks of gestation and babies with birth weight ranging from 0.9 kg to 2.5 kg were included in this study. These were the babies who were admitted in the neonatal intensive care unit and were on high concentration oxygen therapy. The fundi of the babies were examined under sterile conditions using an indirect ophthalmoscope, 20D and 28D lens. Data was analyzed through SPSS version 17.

Results: The mean gestational age of the babies was 30.48 ± 1.517 weeks plus mean birth weight 1.56 ± 0.30 kg. Out of 85 babies 54.1% were males while 45.9% were females. 20 (23.5%) of these babies were found to be suffering from retinopathy of prematurity. Among ROP positive infants, mostly belong to gestational age group 30 weeks and birth weight 1.1 to 1.5 kg group.

Conclusion: Retinopathy of prematurity is a disease of the premature infants. Lower gestational age at birth (less than 34 weeks) and low birth weight (less than 2 kg) have a strong association with development of retinopathy of prematurity. *Al-Shifa Journal of Ophthalmology 2023; 19(2): 77-84. © Al-Shifa Trust Eye Hospital, Rawalpindi, Pakistan.*

-
1. Shifa College of Medicine, Shifa Tameer-e-Millat University.
 2. HBS Medical and Dental College, Ali Pur, Islamabad.
 3. Faisalabad Medical University, Faisalabad.
 4. Gujranwala Medical College, Gujranwala.
 5. Rawalpindi Medical University, Rawalpindi.
-

Originally Received: 05 January 2023

Revised: 27 January 2023

Accepted: 30 January 2023

Correspondence to:

Noor Abbasi

dr_maninoor_abbasi@yahoo.com

Introduction:

The history of retinopathy of prematurity (ROP) is relatively short and it has become one of the most common causes of irreversible childhood blindness in developed and developing countries¹. ROP is a vasoproliferative disorder of the eye affecting preterm infants which can rapidly progress to cause permanent visual impairment or blindness^{1,2}. The worldwide incidence of premature infants who develop ROP is 10.4%^{3,4,5}.

Advances in neonatal care in the last decade, have improved the survival rates for premature infants. Consequently, the incidence of ROP and its complications has increased in parallel^{6,7,8}. In the developed countries, with the progress in neonatology, the survival of infants of low gestational age has increased resulting in an increase in the number of cases of ROP⁹.

Complications of untreated ROP include loss of visual field, strabismus, amblyopia and retinal detachment. Retinal detachment is the most dangerous complication as it causes permanent and irreversible blindness¹⁰.

With the progressively improved neonatal care of premature babies in our country (giving high concentration oxygen therapy), ROP is quite likely to become a significant cause of neonatal blindness. In our country, we do not have sufficient data about the load of ROP in premature infants. Screening of premature infants (either gestational age less than 34 weeks or birth weight less than 2 kg) for retinopathy will result in the timely diagnosis of the disease and so the appropriate management.

Material and Methods:

An institutional cross-sectional study was conducted in the department of Ophthalmology, Holy Family Hospital, Rawalpindi in collaboration with department of Paediatrics, Holy Family Hospital for a duration of 12 months from 1st April, 2018 to 31st March, 2019. . The sample size was 85 and was collected using non probability consecutive sampling technique. 85 babies born before 34 weeks of gestation and babies with birth weight ranging from 0.9 kg to 2.5 kg were included in this study. These were the babies who were admitted in the neonatal intensive care unit and were on high concentration oxygen therapy. Babies suffering from perinatal life-threatening disease (e.g., developmental congenital anomalies involving the central nervous system, cardio-pulmonary system, and gastrointestinal tract), babies having any other congenital eye diseases (e.g., developmental congenital malformation of eye and orbit) or babies with ocular birth trauma were excluded from this study. After informed consent from the parents, the ocular examination of babies was done. This examination was done after 4 weeks of birth. During this time, these babies remained on high ambient oxygen. The

fundi of the babies were examined in detail. Sterile gloves, lid speculum, and forceps were used during the examination. Topical anesthesia was achieved by proparacaine (0.5%) ophthalmic solution. The pupils of the babies were dilated using topical tropicamide and isophrine (2.5%). The babies were swaddled and their fundi were examined using indirect ophthalmoscope, 20D and 28D lens. Fundal findings were noted and entered into a proforma. Data was analyzed through SPSS version 17.

Results:

Sample size was calculated through WHO formula and 85 infants were included in this study. Out of the total 85 infants, 39 (45.9%) were female while 46 (54.1%) were male (Figure 1).

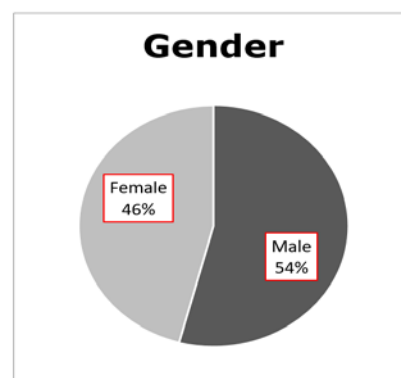


Figure 1: Gender Distribution

The gestational age was taken into account and the mean gestational age of the infants was 30.48 ± 1.517 weeks. 44 infants (51.76%) had gestational age of 30 weeks or less. The highest representation was from the gestational age of 30 weeks which was 22.4%. The rest of the distribution has been given in figure 2.

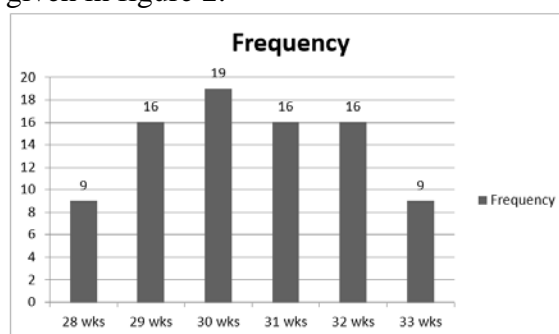


Figure 2: Graph of Gestational age Frequency

The birth weight was taken into account. Mean birth weight was found to be 1.56 ± 0.30 kg. The highest presentation was from birth weight group 1.1 to 1.5 kg which was 59.59%. the rest of the distribution has been given in table 1.

Out of the total of 85 infants, 20 patients (23.5%) were found to be having ROP. Most affected birth weight group and most affected gestational age group plus distribution of ROP in all groups are shown

in table 3 and table 4 respectively. As far as birth weight is concerned, most ROP cases were from group 1.1 to 1.5 kg, 11/85(12.9 %) and among different gestational ages, most ROP cases were from gestational age 30 weeks, 6/85 (7.05%). Rest of the details are in table 2.

Table 1: Frequency of infants falling into different birth weight groups

Birth weight (kg)	Number of infants	Percentage (%)
0.6 -1	6	7.06
1.1-1.5	43	50.59
1.6-2.0	35	7.06
2.1-2.5	1	1.17

Table 2: Frequency of ROP in different birth weights and gestational age groups

Weight (kg)	Number of Infants with ROP	Percentage (%)
0.6-1	4	4.7
1.1-1.5	11	12.9
1.6-2	5	5.9
2.1-2.5	0	0.0
Total	20	23.5
Gestational age (weeks)		
28	1	1.2
29	5	5.9
30	6	7.05
31	3	3.53
32	4	4.7
33	1	1.2
Total	20	23.5

The male babies were slightly more 46 (54.1%) with ratio of 1.18: 1. The study population comprises premature babies with gestation age 28 to 33 years and low birth weight with age range between 0.9 to 2.5 kg. Table 3.

Effect of different variables on incidence of ROP remained like this. Compared with female neonates, incidence of prematurity

are slightly less in male neonates odds ratio .922 95% cl 0.318 to 2.676 however this effect is not significant. We found significant protective impact of weight of the new born on retinopathy of prematurity. The result showed with one kg increase in weight the odds of prematurity are decrease by .126, 95% CL 018 to .860. Table 4

Table 3 characteristics of study population

Variable	a Frequency /Mean (SD)b	a Percentage /minimum-maximum b
Gender new born		
Male	46	54.1%
Female	39	45.9%
Gestational age	30.45 ±1.50	28—33
Weight new born (kg)	1.56 ±0.30	0.9 –2.5 kg

a frequency and percentage for categorical data, b mean standard deviation, minimum and maximum values for quantitative data

Table 4 effect of independent variables on incidence of prematurity

				95 CL		
Independent variable	B	SE	P value	Odds ratio	Lower	Upper
Gender	-.081	.544	.882	.922	.318	2.676
Weight	-2.075	.981	.035	.126	.018	.860
Gestational age	-.007	.180	.967	.993	.697	1.413
Constant	2.303	5.626	.682			

Dependent variable, retinopathy of prematurity coded as 0 no absent 1 present , gender female versus male , weight in kg . Cl confidence interval
Method ENTER

Applied test: logistic regression Analysis

Discussion:

Retinopathy of prematurity is a condition which is strongly associated with prematurity of infants. It's a retinal disease in which abnormal blood vessels grow in retina. It's a treatable cause of blindness in neonates but in Pakistan, ROP is often not recognized early because screening and treatment programs are not yet active in most neonatal units, even in tertiary care hospitals. As far as developed countries are concerned, the premature babies are sought out actively so that the consequences of retinopathy are not the same as we see in the developing countries like ours. Retinopathy of prematurity has decreased over the last decade due to improvement in antenatal care.

Whatever the incidence is, ROP is the major cause of blindness and decreased visual acuity in children in both the developing and developed countries. It has many factors responsible for it. The main associations are decreased gestational age, decreased birth weight and prolonged exposure to oxygen following delivery. Further factors responsible for it are anemia, sepsis, apnoea, male gender, maternal diabetes¹¹.

Our study included 85 patients and it was found that out of these 85 patients, 20 (23.5%) were confirmed to be suffering from retinopathy of prematurity, while 65(76.5%) babies had normal retinas. All of them need further follow ups, and those suffering from ROP need proper management. In a study by Awan A, et al, frequency of retinopathy of prematurity was 3.2 %. This is contrary to our study, where frequency is 23.5% but male female ratio is almost same as ours. Added thing in their study was different treatment approaches according to the stage of the disease, because of which the babies had favorable outcomes¹². Yucel OE, et al included 2186 infants in their study. The overall incidence of any stage of retinopathy and the stage specifically requiring the treatment were found to be 43.5% and 8% respectively. According to

this study, babies with extremely low birth weight and extremely low gestational age had high rate of ROP and also the more severe ROP.¹³

According to -Rauf A, et al, ROP is a serious disease which affects the premature infants and in developing countries, it has become a serious health problem. They concluded by saying that the prevalence of ROP in prematurely delivered babies, who visited Ganga Ram hospital Lahore, is 27%¹⁴.

Quinn GE, et al concluded that 43% of premature infants who were at risk of developing retinopathy of prematurity, developed some stage of the disease and among these mostly recovered without treatment but about 12.5% had severe ROP and these were the infants whose birth weight was less than 1.2 kg. Special thing about this study was that it was a large multicenter study and data was analyzed retrospectively. Its data was collected from 29 hospitals of USA and Canada¹⁵. According to Sohaila A, et al, in their study, 53.5% were males and 46.5% were females which is almost same ratio as in our study and in many other studies. As far as ROP confirmed infants were concerned, their percentage was 10.5% on first eye examination. Adding to this, they concluded that there was a noticeable association between gestational age <32 weeks and birth weight less than 1.5 kg¹⁶. Almost similar results and conclusion were made by Kaur H And Kal S¹⁷. This shows that these studies had similar results as ours.

Hong EH, et al reviewed previous researches and gave a key message that in past there were global tri-phasic epidemic times of ROP. They further added that in recent times, its incidence has been between 10% and 40% which depends upon the country and the study population. This review article also stressed upon the timely ROP screening and specific treatments according to the stage of the disease so that the progression of the disease and its complications can be

prevented¹⁸. A study from South Korea included 141,964 premature infants. Among them, nationwide incidence of ROP was found to be 29.8%. This incidence in gestational age group of <28 weeks was 4.3 times higher than in gestational age 28-37 weeks. This was the first Korean nationwide epidemiological study of ROP which revealed that the incidence of retinopathy of prematurity has decreased in infants undergoing conventional treatment during an 11 years' time, from 2007(4.7%) to 2018(1.8%)¹⁹.

Wu T, et al conducted a retrospective study in China and determined the incidence and perinatal risk factors for retinopathy of prematurity in very low-birth-weight infants. For this, medical records of infants, who were screened for ROP from 2012 to 2015, were checked. 26.0% was the overall incidence of ROP (131/504). Among perinatal risk factors, GA < 32 weeks was the most important risk factor. Others were sepsis, patent ductus arteriosus, in vitro fertilization and blood transfusion²⁰.

Similar to our study, a prospective observational study was carried out at Princess Marina Hospital in Gaborone, Botswana. Infants with gestational age less than 34 weeks or infants with birth weight less than 1.8 kg were included in this study. 200 premature infants were screened for ROP. Among these, 22 were found to be having the disease with the incidence of 11%. This study showed a significant association between risk factors (birth weight, gestational age and blood transfusion) and the disease²¹.

Limitation of our study was that it couldn't be carried out on large scale because of difficulty in engaging the concerned people of other hospitals but its comparable to those studies which were carried out on infants from multiple centers. That's why we expect that hopefully this study will be useful in timely diagnosis and formulation of newer guidelines so that the disease prevention and timely diagnosis and so the appropriate management can be done.

Conclusion:

Retinopathy of prematurity is a serious disease of the premature infants in Pakistan. Although the sample size was small and we made the limited observations but still the results show an important association of ROP with low gestational age and low birth weight. All Premature infants with risk factors should have serial eye examinations for timely diagnosis and management.

Recommendations:

Awareness needs to be increased among all concerned doctors and parents of premature infants. Many studies, including our study, have been done on a small sample of the population so there is a need for conducting large multi-centre studies to determine the true incidence of ROP in Pakistan and to formulate cost-effective, region-specific screening guidelines for ROP.

References:

1. Disher T, Cameron C, Mitra S, Cathcart K, Campbell-Yeo M. Pain-Relieving Interventions for Retinopathy of Prematurity: A Meta-analysis. *Pediatrics*. 2018;142(1).doi: 10.1542/peds.2018-0401.
2. Hajrasouliha AR, Garcia-Gonzales JM, Shapiro MJ, Yoon H, Blair MP. Reactivation of Retinopathy of Prematurity Three Years After Treatment with Bevacizumab. *Ophthalmic Surg Lasers Imaging Retina*. 2017;48(3):255-9.doi: 10.3928/23258160-20170301-10.
3. Kim SJ, Port AD, Swan R, Campbell JP, Chan RVP, Chiang MF. Retinopathy of prematurity: a review of risk factors and their clinical significance. *Surv Ophthalmol*. 2018;63(5):618-37.doi: 10.1016/j.survophthal.2018.04.002. Epub 2018 Apr 19.
4. Ludwig CA, Chen TA, Hernandez-Boussard T, Moshfeghi AA, Moshfeghi DM. The Epidemiology of Retinopathy of Prematurity in the United States.

- Ophthalmic Surg Lasers Imaging Retina. 2017;48(7):553-62.doi: 10.3928/23258160-20170630-06.
5. Dogra MR, Katoch D, Dogra MJTIJoP. An update on retinopathy of prematurity (ROP).Indian J Pediatr. 2017;84(12):930-6. DOI: [10.1007/s12098-017-2404-3](https://doi.org/10.1007/s12098-017-2404-3)
 6. Mintz-Hittner HA, Geloneck MM, Chuang AZ. Clinical Management of Recurrent Retinopathy of Prematurity after Intravitreal Bevacizumab Monotherapy. Ophthalmology. 2016;123(9):1845-55.doi: 10.1016/j.ophtha.2016.04.028. Epub 2016 May 27.
 7. Rivera JC, Holm M, Austeng D, Morken TS, Zhou TE, Beaudry-Richard A, et al. Retinopathy of prematurity: inflammation, choroidal degeneration, and novel promising therapeutic strategies. J Neuroinflammation. 2017;14(1):165.doi: 10.1186/s12974-017-0943-1.
 8. Higgins RD. Oxygen saturation and retinopathy of prematurity. Clin Perinatol.2019;46(3):593-9. DOI: [10.1016/j.clp.2019.05.008](https://doi.org/10.1016/j.clp.2019.05.008)
 9. Bashinsky AL. Retinopathy of prematurity. N C Med J. 2017;78(2):124-8.doi: 10.18043/ncm.78.2.124.
 10. Hamad AE, Moinuddin O, Blair MP, Schechet SA, Shapiro MJ, Quiram PA, et al. Late onset retinal findings and complications in untreated retinopathy of prematurity. Ophthalmol Retina.2020 Jun;4(6):602-612.doi: 10.1016/j.oret.2019.12.015.
 11. Wallace DK, Kraker RT, Freedman SF, Crouch ER, Hutchinson AK, Bhatt AR, et al. Assessment of lower doses of intravitreal bevacizumab for retinopathy of prematurity: a phase 1 dosing study. JAMA Ophthalmol. 2017;135(6):654-6.doi: 10.1001/jamaophthalmol.2017.1055.
 12. Awan MA, Haq A, Shaheen F, Nazir S, Choudhry S. Frequency and outcome of retinopathy of prematurity at tertiary care hospital in Pakistan. J Coll Physicians Surg Pak. 2022 Jul;32(7):895-89. doi: 10.29271/jcpsp.2022.07.895
 13. Yucel OE, Eraydin B, Niyaz L, Terzi O. Incidence and risk factors for retinopathy of prematurity in premature, extremely low birth weight and extremely low gestational age infants. BMC Ophthalmology. 2022;22(1):367. DOI: [10.1186/s12886-022-02591-9](https://doi.org/10.1186/s12886-022-02591-9)
 14. Rauf A, Saigol HK, Chauhan K, Akbar S, Chaudhary NI. Prevalence of retinopathy of prematurity in premature neonates visiting Sir Gangaram hospital, Lahore. Pakistan journal of medical and health sciences. 2023;17(2):206-208. DOI: <https://doi.org/10.53350/pjmhs2023172206>
 15. Quinn GE, Ying G, Bell EF, et al. Incidence and early course of retinopathy of prematurity. Secondary Analysis of postnatal growth and retinopathy of prematurity (G-ROP) study. JAMA Ophthalmol. 2018;136(12):1383-1389.doi: 10.1001/jamaophthalmol.2018.4290.
 16. Sohaila A, Tikmani SS, Khan IH,Atiq H, Akhter ASM, Kumar P, et al.Frequency of retinopathy of prematurity in premature neonates with a birth weight below 1500 grams and a gestational age less than 32 weeks: A study from a tertiary care hospital in a lower-middle income country.PLoS One. 2014;9(7):e100785.doi: 10.1371/journal.pone.0100785. eCollection 2014.
 17. Kaur H, Kai S. Prevalence of retinopathy of prematurity among premature babies in a tertiary care hospital. International Journal of research in medical sciences. 2023;11(1):113-117.DOI: <https://doi.org/10.18203/2320-6012.ijrms20223301>
 18. Hong EH, Shin YU, Cho H. Retinopathy of prematurity: a review of epidemiology and current treatment

- strategies. *Clinical and Experimental Pediatrics*. 2022;65(3):115-126.doi: [10.3345/cep.2021.00773](https://doi.org/10.3345/cep.2021.00773)
19. Hong EH, Shin YU, Bae GH, Choi YJ, Ahn SJ, SobrinL,et al. Nationwide incidence and treatment pattern of retinopathy of prematurity in South Korea using the 2007-2018 national health insurance claims data. *Scientific Reports*. 2021;11:1451. doi: [10.1038/s41598-021-80989-z](https://doi.org/10.1038/s41598-021-80989-z).
20. Wu T, Zhang L, Tong Y, Qu Y, Mu Dezhi. Retinopathy of prematurity among very low-birth-weight infants in China: Incidence and perinatal risk factors. *Retina*. February 2018;59:757-763. DOI: [10.1167/iovs.17-23158](https://doi.org/10.1167/iovs.17-23158)
21. Gezmu AM, Quinn GE, Nkomazana O, Nqubula JC, Joel D, Banda FM,et al. Incidence of retinopathy of prematurity in Botswana:A prospective observational study.2020;14:2417-2425. doi: [10.2147/OPHTH.S265664](https://doi.org/10.2147/OPHTH.S265664)

Authors Contribution

Concept and Design: Kanwal Zareen Abbasi
Data Collection / Assembly: Muhammad Rizwan Khan
Drafting: Munib Ur Rehman, Maria Zubair
Statistical expertise: Fuad Ahmad Khan Niazi
Critical Revision: Bilal Humayun Mirza