

ORIGINAL ARTICLE

Prevalence of Retinopathy of Prematurity in Premature Neonates Visiting Sir Gangaram Hospital LahoreABDUL RAUF¹, HUMA KAYANI SAIGOL², KHURRAM CHAUHAN³, SEEMAB AKBAR⁴, NAJAM IQBAL CHAUDHARY⁵¹Senior Registrar, Department of Ophthalmology, Sir Gangaram Hospital, Lahore Pakistan²Professor & Head, Department of Ophthalmology, Sir Gangaram Hospital/ Fatima Jinnah Medical University, Lahore Pakistan^{3,4}Senior Registrar, Department of Ophthalmology, Sir Gangaram Hospital, Lahore Pakistan⁵Assistant Professor, Department of Ophthalmology, Sir Gangaram Hospital/ Fatima Jinnah Medical University, Lahore PakistanCorresponding author: Abdul Rauf, Email: drabdulrauf181@gmail.com**ABSTRACT****Background:** Retinopathy of prematurity (ROP) is a serious problem which affects the premature infants. It is becoming a public health issue in developing countries like Pakistan. Antenatal visits, delivery and NICU management plays an important role in prevention of ROP.**Objective:** The aim of this study was to find out the prevalence of retinopathy of prematurity in premature neonates visiting Sir Ganga Ram hospital Lahore.**Study Design:** observational study.**Settings:** Study was carried out in Out-patient of Ophthalmology Department, A public sector Sir Ganga Ram Hospital, Lahore Pakistan.**Duration:** The duration of the study was one year from September 2020 to August 2021.**Methods:** All the preterm babies referred from pediatric department were part of study. A total of 160 babies were examined in this study. The data was presented in the form of frequency and percentages using SPSS software.**Results:** In this study out of 160 patients 75(46.87%) were male and 85(53.12%) were females. The prevalence of retinopathy of prematurity was observed in 43(26.87%) babies. Weight of patients less than 1kg was 11(25.58%) between 1-1.5 kg was noted in 28(65.11%) patients and >2 kg weight was noted in 4(9.30%) patients. Babies with ROP, 23(53.48%) recovered without any intervention, 9(20.93%) required intervention and recovered after 3 months follow up, 6(13.95%) kept under observation and recovered after 4 months and 5(11.62%) babies lost follow up.**Practical implication:** this study will help in early diagnosis and prevention of disease and help to formulate and introduce newer guidelines for prevention, early identification and prompt treatment starting from basic levels to prevent development of ROP of any stage.**Conclusion:** The study concluded that the prevalence of retinopathy of prematurity in premature neonates visiting Sir Ganga Ram hospital Lahore is 27%.**Keywords:** Retinopathy of Prematurity(ROP), Neonates, Preterm, screening, blindness**INTRODUCTION**

Retinopathy of prematurity (ROP) is a disease of retinal vascular and capillary proliferation affecting preterm infants undergoing oxygen therapy.¹ ROP is one the major problem of neonates having premature gestational age which could lead to visual impairment and complete blindness. It is the major cause of major cause of childhood blindness,^{2,3} which is becoming a public health issue in developing countries like Pakistan due to increase number of preterm births along with increasing NICU facilities.⁴

ROP results from oxygen requirement which in turn results in pathologic growth of vessels in the developing retina that may lead to permanent damage to the retina as well as retinal detachment and macular folds.¹ Severity of ROP is associated with duration of oxygen therapy.^{5,6} Early diagnosis and early management can help in preventing this major cause of blindness. This will not only reduce the disease burden but also decrease the health facilities expenses for this disease.

Among low birth or premature infants, screening for ROP is important and crucial. Guidelines from the American Academy of Ophthalmology, American Academy of Pediatrics, and the American Association for Pediatric Ophthalmology and Strabismus state that infants born ≤ 30 weeks gestational age (GA) or ≤ 1500 g BW should be screened for ROP. Depending on the clinical course, larger infants may benefit from screening as well.^{7,8} In ROP, NICU management and antenatal visits plays key role in prevention of ROP. Antenatal visits, delivery and NICU management plays an important role in prevention of ROP.¹⁰ Overall not more than 10% infants who undergo screening examinations require treatment.⁹

A local study done by Mayd Riaz and co-workers in 2019 conducted a cohort study at Hameed Latif Hospital Lahore where all the neonates having low birth weight and gestational age were examined. It showed that 28 % of those screened had developed ROP.⁵ Similarly one cross sectional study done in Tehran, Iran by Khorsdifar Milad et al⁶ reported the incidence of ROP as 33.3%.

The author of this study showed that low gestational age, low birth weight, Intraventricular hemorrhage and patent ductus arteriosus are the contributing factor for development of ROP.⁶ Another cohort study done in Iran also demonstrated in their study findings that the prevalence of ROP was 27.28%. This study also showed the low gestational age, low birth weight and history of blood transfusion at time of birth are strongly associated with the ROP.¹¹ One study in China enrolled extreme low birth weight children from period of 2004 to 2018. They enrolled 1099 infants in which 50.7% had RP and 29.9% had severe ROP.¹²

Retinopathy of prematurity is one of the leading causes of permanent blindness. A huge number of infants are born prematurely and are at increased risk of developing the disease in the countries like Pakistan, where there is a lack of facilities and expertise on the identification, risk factors and management strategies regarding ROP. This not only affects the patient by rendering him/her blind for life but also a huge burden on health facilities as well as economical set back on individual and national level. There is not much data available at local level on ROP, which is a preventable cause of blindness. There is an utmost need to formulate and introduce newer guidelines for prevention, early identification and prompt treatment starting from basic levels to prevent development of ROP of any stage.

METHODS

The observational cross-sectional study done in a public sector Sir Ganga Ram hospital Lahore. Total 160 preterm babies who were less than 35weeks and weight less than 2000grams were referred from pediatric department were enrolled in this study by using consecutive sampling technique. The duration of the study was one year from September 2020 to August 2021. This study was done in Out-patient of Ophthalmology department of Sir Ganga Ram Hospital, Lahore.

All the patients referred from pediatric department were part of study. Preterm infants with gestational age <30 weeks at birth, Infants who underwent supplemental oxygen therapy within 1 week of birth and Infants with birth weight less than 2000 grams at birth included in study.

Verbal informed consent from parents of infants for examination was taken. The infant was examined after complete dilatation of pupils with cyclopentolate eye drops 5ml, Phenylephrine eye drops 2.5ml and tropicamide eye drops 2.5ml combination. Detailed funduscopy using indirect ophthalmoscope with 28D lens with scleral indentation done to see the zone, stage and pre plus or plus status of disease. If there was no ROP then follow up done after 2 weeks and if after 2 weeks still no change then no further examination needed. If seen stage 1 and stage 2 then weekly follow up till it regressed. If stage 3 or pre plus requiring intervention, then treatment given and kept on follow up weekly till its regression. The independent variables of the study were gender, gestational age and birth weight while the dependent variables were ROP and recovery status of the infants. The treatment options given to each infant and effect of every treatment. The prevalence, pattern of disease progression and efficacy of treatment options was evaluated and noted. The data was collected on a predesigned performa.

All the collected data was entered and analyzed on SPSS version 26. Qualitative data was presented in the form of frequency and percentages and quantitative were presented in the form of mean ± SD.

RESULTS

In this study total number of referred patients from Pediatric department was 254 in which 160 patients were examined in which 75(46.87%) were males and 85(53.12%) were females and rest didn't shown up. Out of 160 patients 117 had no ROP. The ROP was observed in 43(26.87%) patients in which 22(51.16%) were males and 21(48.83%) were females. Among patients with ROP 23(53.48%) recovered without any intervention from 2 weeks to 3 months follow up, 6(13.95%) kept under observation and they recovered after 3 months follow up, 5(11.62%) lost follow ups and 9(20.93%) patients needed intervention. 3(33.33%) out of 9 underwent argon laser photocoagulation for two times kept under follow up and recovered after 3months. Another 3(33.33%) got intravitreal Anti VEGF Bevacizumab 0.62mg/0.025mg one month apart. All these 3 patients got total 2 injections and became stable after 3 months follow up. Rest of 3(33.33%) got combined argon laser and Anti VEGF and became stable after 3 months follow up. The follow up was done on weekly basis and on each follow up thorough examination was done to look for zone, stage, pre plus, plus and regression of blood vessels

Table 1: Gender distribution of patients (%) n=160

Gender	Frequency (n)	Percentage (%)
Male	75	46.87
Female	85	53.12

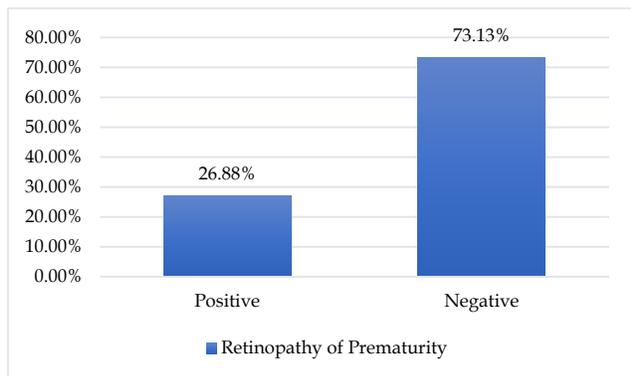


Figure 1: Prevalence of retinopathy of prematurity n=160

Table 2: Distribution of patients by weight (kg) n=160

Weight of patients (kg)	No of patients	Percentage (%)
1-1.5	11	25.58%
1.5-2	28	65.11%
>2	4	9.30%

Table 3: Distribution of gestational age in weeks (n=43)

Gestational age(weeks)	No. of patients	Percentage (%)
<28	4	9.32%
28-30	25	58.13%
31-32	6	13.95%
33-34	4	9.32%
>34	4	9.32%

Table 4: Stage wise distribution of patients (n=43)

Stage	No. of patients	Percentage
Stage 1	9	(5.5%)
Stage 2 without plus	25	(16%)
Stage 2 with plus disease	1	(0.6%)
Stage 3 with plus disease	8	(4.9%)
Stage 4 and 5	None	None

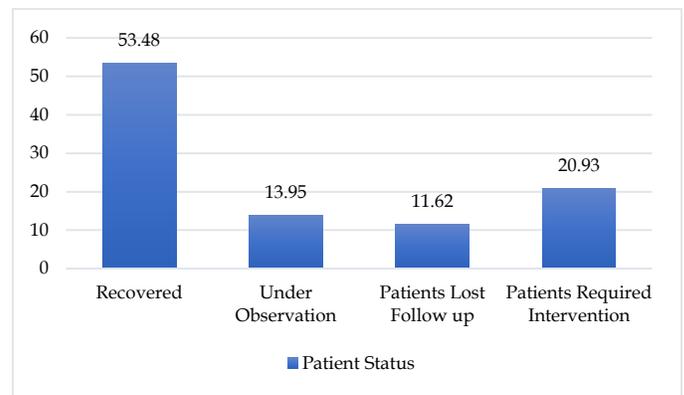


Figure 2: Distribution of ROP patients status by screening (n=43)

Table 5: Distribution of patients by treatment (n=9)

Treatment given	No. of patients	Percentage (%)
Argon laser application	3	33.33%
Intravitreal Anti VEGF	3	33.33%
Combination of laser and injection	3	33.33%

DISCUSSION

Retinopathy of prematurity is a serious problem which affects the premature infants. It's a worldwide prevalent disease. Mostly mild ROP regresses without any intervention but in severe cases this problem may lead to visual impairment. It primarily occurred in extremely low birth weight infants.^{13,14}

Similar to our study findings were reported in one study in Singapore which showed the incidence of ROP in extremely low birth weight babies as 29.2% having median gestational age of onset as 35 week (31-40 week).¹⁵ Another study results were similar to that of study. One study in India also showed the consistent results to our study. Murthy KR et al¹⁶ in India reported prevalence of ROP in 24% patients. Whereas a study done by Taqui AM¹⁷ in Pakistan reported a higher prevalence of ROP. In this Pakistani study the ROP prevalence was 32.4%.¹⁷ This can be explained by the fact that these studies involved only very low birth weight infants. Another local study done by Mayd Riaz and co-workers in 2019 conducted a cohort study at Hameed Latif Hospital Lahore where all the neonates having low birth weight and gestational age combined were examined. It showed that 28 % of those screened had developed ROP.⁵ Study done in Beijing by Chen Y et al showed very low prevalence of ROP as compared to our study, The author of this study reported a prevalence of

10.8% patients but he enrolled patients having higher gestational age and higher birth weight.¹⁸

In China, a retrospective cohort study was conducted by Prudence P. and others at Prince of Wales Hospital. 754 infants were included in the study from January 2006 to December 2015. 31% patients had developed ROP. Two yearly trend of incidence was seen. It was observed that there is a decrease in the incidence of ROP over 2 yearly period for any type of ROP. However, no significant change in the trend of ROP type 1 was observed over time.¹⁹

Another retrospective Cohort study was carried out in South Korea to assess the local incidence and treatment pattern for ROP. An overall incidence of 29.8% was observed. The incidence was found to be 4.3 times higher in infants having gestational age if < 28 weeks as compared to those between 28 to 37 weeks. The overall trend of incidence decreased from 39.5% to 23.5% over a duration of 12 years. The percentage of ROP patients who underwent treatment was observed to fall from 4.7% in 2007 to 1.8% in 2018.²⁰

On the other hand a meta analysis done in Iran showed very low prevalence of ROP as compared to our study. This meta-analysis showed that prevalence of prematurity was 9.2% (95% CI: 7.6–10.7)²¹ This difference may be due to the difference in study setting and study type.

Tabarez-Carvajal et al enrolled 3018 premature infants in their study. In their study stage 1 ROP was observed in 8.34%, stage 2, 3, 4 & 5 was observed in 8.78%, 1.9%, 0.03%, and 0.30% patients respectively.²² Abdel HA et al enrolled 172 infants in their study in which 33(19.2%) infants developed ROP either in one eye or both eyes. The author reported that at stage 1 the prevalence of ROP was 10.4%, the prevalence of ROP at stage 2 was 5.2% and prevalence at stage 3 was noted in 3.45%, no patients reported in their study having stage 4 & 5.²³

In future further study should be done in addition of many other factors. It is suggested that in future studies should be done at multicenter setting rather than to a single center setting to control the bias.

CONCLUSION

The study concluded that the prevalence of retinopathy of prematurity in premature neonates visiting Sir Ganga Ram hospital Lahore is 27%.

Limitations: The limitation of the current study was a single center study.

Suggestions / Recommendations: A multi-centered study with a larger sample size should be conducted so that the results should be generalized within the population with better efficacy of results.

Conflict of Interest / Disclosure: The author declare no conflict of interest.

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REFERENCES

- Brown AC, Nwanyanwu K. Retinopathy Of Prematurity. StatPearls [Internet]. 2021.
- Hansen ED, Hartnett ME. A review of treatment for retinopathy of prematurity. Expert review of ophthalmology. 2019;14(2):73-87.
- Azami M, Jaafari Z, Rahmati S, Farahani AD, Badfar G. Prevalence and risk factors of retinopathy of prematurity in Iran: a systematic review and meta-analysis. BMC ophthalmology. 2018;18(1):1-14.
- Dogra MR, Katoch D. Retinopathy of Prematurity: An emerging and evolving challenge. Indian journal of ophthalmology. 2017;65(9):782.
- Zhu Z, Hua X, Yu Y, Zhu P, Hong K, Ke Y. Effect of red blood cell transfusion on the development of retinopathy of prematurity: A systematic review and meta-analysis. PLoS One. 2020;15(6):e0234266.
- Stritzke A, Kabra N, Kaur S, Robertson HL, Lodha A. Correction to: Oral propranolol in prevention of severe retinopathy of prematurity: a systematic review and meta-analysis. Journal of perinatology : official journal of the California Perinatal Association. 2019 Dec;39(12):1695.
- Fierson WM. Screening Examination of Premature Infants for Retinopathy of Prematurity. Pediatrics. 2018 Dec;142(6).
- Cagliari PZ, Lucas VC, Borba IC, Leandro DMK, Gascho CL, Veras TN, et al. Validation of ROPScore to predict retinopathy of prematurity among very low birth weight preterm infants in a southern Brazilian population. Arquivos Brasileiros de Oftalmologia. 2019;82:476-80.
- Quinn GE, Ying G-s, Bell EF, Donohue PK, Morrison D, Tomlinson LA, et al. Incidence and early course of retinopathy of prematurity: secondary analysis of the postnatal growth and retinopathy of prematurity (G-ROP) study. JAMA ophthalmology. 2018;136(12):1383-9.
- Roberts D, Brown J, Medley N, Dalziel SR. Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth. Cochrane Database Syst Rev. 2017 Mar 21;3(3):CD004454.
- Zarei M, Bazvand F, Ebrahimiadib N, Roohipoor R, Karkhaneh R, Dashtjani AF, et al. Prevalence and risk factors of retinopathy of prematurity in Iran. Journal of ophthalmic & vision research. 2019;14(3):291.
- Zhang G, Yang M, Wu Z, Lam W, Lian C, Zhao G, et al. Changes in the incidence of retinopathy of prematurity in extremely low birth weight infants in South China from 2004 to 2018. Ophthalmic Epidemiology. 2021;28(4):359-64.
- Lundgren P, Stoltz Sjöström E, Domellöf M, Källén K, Holmström G, Hård A-L, et al. WINROP identifies severe retinopathy of prematurity at an early stage in a nation-based cohort of extremely preterm infants. PLoS One. 2013;8(9):e73256.
- Anuk-Ince D, Gülcan H, Hanta D, Ecevit A, Akkoyun İ, Kurt A, et al. Poor postnatal weight gain predicts stage 3+ retinopathy of prematurity in very low birth weight infants. Turk J Pediatr. 2013;55(3):304-8.
- Shah V, Yeo C, Ling Y, Ho L. Incidence, risk factors of retinopathy of prematurity among very low birth weight infants in Singapore. Ann Acad Med Singapore. 2005;34(2):169-78.
- Murthy KR, Babu K, Benakappa N, Murthy PR. Analysis of risk factors for the development of retinopathy of prematurity in preterm infants at a tertiary referral hospital in South India. Acta Medica Lituanica. 2006;13(3).
- Taqi AM, Syed R, Chaudhry TA, Ahmad K, Salat MS. Retinopathy of prematurity: frequency and risk factors in a tertiary care hospital in Karachi, Pakistan. Journal of the Pakistan Medical Association. 2008;58(4):186.
- Chen Y, Li X, Yin H, Gilbert C, Liang J, Jiang Y, et al. Risk factors for retinopathy of prematurity in six neonatal intensive care units in Beijing, China. British Journal of Ophthalmology. 2008;92(3):326-30.
- Chow PP, Yip WW, Ho M, Lok JY, Lau HH, Young AL. Trends in the incidence of retinopathy of prematurity over a 10-year period. International Ophthalmology. 2019;39(4):903-9.
- Gol S, Pena RN, Rothschild MF, Tor M, Estany J. A polymorphism in the fatty acid desaturase-2 gene is associated with the arachidonic acid metabolism in pigs. Scientific reports. 2018;8(1):1-9.
- Vakilian K, Ranjbaran M, Khorsandi M, Sharafkhani N, Khodadost M. Prevalence of preterm labor in Iran: a systematic review and meta-analysis. International Journal of Reproductive BioMedicine. 2015;13(12):743.
- Tabarez-Carvajal AC, Montes-Cantillo M, Unkrich KH, Trivedi RH, Peterseim MMW. Retinopathy of prematurity: screening and treatment in Costa Rica. British Journal of Ophthalmology. 2017;101(12):1709-13.
- Abdel HA, Mohamed G, Othman M. Retinopathy of prematurity: a study of incidence and risk factors in NICU of Al-Minya University Hospital in Egypt. Journal of Clinical Neonatology. 2012;1(2):76.