

Factors Associated with Retinopathy of Prematurity in Hospitalized Preterm Infants in Sanandaj, IranMajid Mansouri¹, Sirous Hemmatpour², Fouzieh Sedighiani³, Mojgan Ghamari⁴, Delnia Chavoshi⁵¹ MD, Associate Professor, Pediatric Department, Kurdistan University of Medical Sciences, Sanandaj, Iran² MD, Assistant Professor, Kurdistan University of Medical Sciences, Sanandaj, Iran³ MD, Ophthalmologist, Towhid Hospital, Kurdistan University of Medical Sciences, Sanandaj, Iran⁴ MD, Kurdistan University of Medical Sciences, Sanandaj, Iran⁵ M.Sc. in Neonatal Intensive Care Nursing, Kurdistan University of Medical Sciences, Sanandaj, Iran**Type of article:** Original**Abstract**

Introduction: In the near future, retinopathy of prematurity (ROP) will be the most significant cause of blindness in upper and middle-income countries. Due to the increasing survival chances for premature and low birth weight infants and the importance of the diagnosis and treatment of ROP, this study was aimed at determining the prevalence of ROP and its related factors in Sanandaj, Iran, in 2014.

Methods: This cross-sectional study was performed on 47 preterm infants, weighing less than 2000 g or with a gestational age of less than 34 weeks. The sampling method was census. From the first examination to 1 to 4 weeks later, until retinal vascularization completion, examinations were performed by the same ophthalmologist. Data were analyzed using SPSS version 20 and frequency, mean, SD and Chi-square tests.

Results: The prevalence of ROP in the infants was 10.6%. Prevalence among girls was 16% and among boys it was 4.5%. The results showed that 23.5% of infants with ROP needed mechanical ventilation. The difference between the two groups was statistically significant ($p = 0.031$).

Conclusion: In this study, the prevalence of ROP in the NICU and neonatal ward of Besat Hospital in Sanandaj was low. However, due to serious consequences of the disease in premature infants, timely screening, determination, and control of risk factors provided necessary support to manage the disease.

Keywords: Retinopathy; Prematurity; Retinopathy of Prematurity; ROP; Retrolental Fibroplasia

1. Introduction

Retinopathy of premature infants which was previously known as, retrolental fibroplasia, is a vascular proliferation retinopathy which forms due to vascular proliferation in a retina that has not completed its vascularization, leading to different outcomes, which vary from normal vision blindness (1). According to the World Health Organization in 2020, retinopathy of prematurity will be the most important cause of blindness in upper and middle-income countries (2). Although the guidelines to improve the classification and treatment of ROP has been conducted, ROP is still a leading cause of reversible blindness in children, especially in developing countries (3). Currently, retinopathy of prematurity is one of the causes of childhood blindness in the United States and Europe (4). Recent advances have improved the survival rate of premature infants and this has led to an increase in retinopathy of prematurity (5). The pathogenicity of ROP is multifactorial and includes two phases. Due to the possibility of hyperoxia, phase 1 occurs typically between 22-30 weeks of gestational age and phase 2 occurs between 31-34 weeks of gestational age (6). The major risk factors for this disease include; low birth weight, gestational age (6), oxygen therapy, genetic factors, multifetal gestation, fungal infections, and bacteremia (7). The impact of the direct costs of the disease include medical attention, counseling, treatment by surgery and laser; as well as, indirect costs including rehabilitation programs, care by parents, the loss of patient's efficiency, and any other support services. These factors show the importance of screening and early detection in high prevalence areas (8, 9). Due to the

Corresponding author:

Assistant Professor Dr. Sirous Hemmatpour, Kurdistan University of Medical Sciences, Sanandaj, Iran.

Tel/Fax: +98.8733285915, Email: Dr.s.hemmatpour@gmail.com

Received: May 02, 2016, Accepted: July 25, 2016, Published: September 2016

iThenticate screening: July 24, 2016, English editing: August 24, 2016, Quality control: September 01, 2016

© 2016 The Authors. This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

increasing survival chances for premature and low birth weight infants, and the importance of the diagnosis and treatment of retinopathy of prematurity, this study was aimed at determining the prevalence of retinopathy of prematurity and related factors in Sanandaj.

2. Material and Methods

The project (code: MUK.REC.1392.212) has been studied and approved in the Ethic Committee, Kurdistan University of Medical Sciences. The examination used in this study is essential in order to prevent blindness in premature babies. It is carried out routinely with caution and without any harm to the baby. This cross-sectional study was performed on 47 preterm infants weighing less than 2000 g or a gestational age of less than 34 weeks. They were hospitalized in the NICU and neonate ward of Besat Hospital in Sanandaj, Iran from October 2013 to October 2014. The sampling method was census. Information on age, sex, weight, gestational age, oxygen concentration and duration of oxygen therapy, frequency of blood transfusion, need for mechanical ventilation and the results of ophthalmology examinations were extracted. All infants were examined by an ophthalmologist and the results were explored in detail. Examination was performed by an ophthalmologist using a HEINE indirect ophthalmoscope, based on the development of retinal vessels. From the first examination to 1 to 4 weeks later, when retinal vascularization reached completion, examinations were performed by the same ophthalmologist. Data were analyzed using IBM© SPSS© Statistics version 20 (IBM© Corp., Armonk, NY, USA) and frequency, mean, SD and Chi-square tests.

3. Results

The results showed that from 47 preterm infants, 25 (53.2%) were girls. The mean and standard deviation of birth weight was 1580 ± 320 grams and the mean and standard deviation of gestational age was 31.6 ± 2.54 weeks. The prevalence of ROP in the infants was 10.6%. Prevalence among girls was 16% and among boys it was 4.5% (Table 1). In this study, 3 patients suffered from Grade 1 ROP and 2 patients were suffering from Grade 2 and 3 ROP. The mean gestational age and birth weight in patients without retinopathy of prematurity were higher than the group with ROP. However, the duration of oxygen therapy and oxygen concentrations in patients with ROP were greater than the group without ROP. The results showed that 23.5% of infants with ROP required mechanical ventilation. The difference between two groups was statistically significant ($p = 0.031$) (Table 1).

Table 1. The relationship between retinopathy of prematurity and the need for mechanical ventilation in terms of infant's gender

Variables		Retinopathy of prematurity; n (%)		p-value
Gender	Female	4 (16)	21 (84)	0.216
	Male	1 (4.5)	21 (95.5)	
The need for mechanical ventilation	Yes	4 (23.5)	13 (76.5)	0.031
	NO	1 (3.3)	29 (76.7)	
	Total	5	42	

4. Discussion

The incidence of premature births is increasing worldwide and consequently ROP is also on the rise (10). Recent estimates indicate that the incidence of ROP, blindness, and severe vision disorders are increasing worldwide (11). Vision problems, including retinal disorders resulting from prematurity are the most common causes of acquired low vision in low birth weight babies. They may lead to blindness without early diagnosis and timely treatment of severe ROP (12). The incidence of severe ROP requiring treatment in South American and Asian countries is more common than western countries (12). ROP is a major cause of blindness in infants and in many cases is predictable and curable (13). Regarding the significant increase in the survival rate of premature infants and high prevalence of ROP in the Eastern Mediterranean area and the need for more information on risk factors, this study was conducted to determine the prevalence of retinopathy of prematurity and its related factors in Sanandaj, Iran (14). In this study, the prevalence of ROP in infants was 10.6%. Three cases suffered from Grade 1 ROP and 2 patients suffered from Grade 2 and 3 ROP. The prevalence of ROP is variable within the country (Iran); as well as, among different countries in the world. In a study in Turkey, frequencies of regular and severe cases of ROP were 28.2 % and 5.8%, respectively (15). In another study which was conducted in Bahrain, from 1,795 preterm infants, ROP was identified in 20.4% of infants from 2002 to 2011 (15). The results of a Ghaseminejad et al. study showed that from 83 premature infants in the central hospital of Kerman, Iran, 24 infants (29%) were diagnosed with ROP (16). Abrishami et al, in a study that was conducted in Mashhad, Iran, showed that the incidence of ROP was 26.2% (17). However, the prevalence of ROP in our study was lower than the studies shown above. In a Fayaz et al. study, which

was conducted on 399 infants who were admitted to neonatal intensive care of Alzahra Hospital in Tabriz, Iran, during 2005-2006, 29 cases (7.27%) were identified as ROP (18), which was lower than the findings of our study. In the present study, the average gestational age and birth weight in the group without ROP were higher than the group with ROP. These results were consistent with the findings of other studies (19). Also in this study, the mean of oxygen duration and oxygen concentrations in the group with ROP was higher than the group without ROP. These findings were similar to the studies of Chen in China (20), Ghaseminejad in Kerman (16) and Abrishami in Mashhad (17). The results showed that between the two groups of ROP and non ROP, there was a statistically significant difference in terms of mechanical ventilation ($P = 0.031$). Bayat Mokhtari et al. reported that, there are meaningful variables to increase the rate of ROP including: mean duration of oxygen therapy, birth weight, and mechanical ventilation (17). These results were also consistent with our study. In a study conducted by Molina et al., using data of three cohort studies in Spain, genetics, environment, and chance were responsible for 78.8%, 23.8% and 4.12% of ROP cases, respectively. Among the environmental factors, the number of intubation days, postpartum weight gain and sepsis were the highest risk factors for ROP, respectively (21). One limitation of this research project is its relatively small sample size, which occurred despite allocation of the majority of preterm infants in the province.

5. Conclusions

In this study, the results showed that there was a statistically significant difference in terms of mechanical ventilation between the two groups of ROP and non ROP. The prevalence of ROP in the NICU and neonatal ward of Besat Hospital in Sanandaj was low. However, due to serious consequences of the disease in premature infants, it is recommended to use timely screening, determination, and control of risk factors to provide necessary support to prevent the disease.

Acknowledgments:

Authors would like to thank the Deputy of Research, Kurdistan University of Medical Sciences, for their financial support.

Conflict of Interest:

There is no conflict of interest to be declared.

Authors' contributions:

All authors contributed to this project and article equally. All authors read and approved the final manuscript.

References:

- 1) Fouladinejad M, Motahari MM, Gharib MH, Sheishari F, Soltani M. The prevalence, intensity and some risk factors of retinopathy of premature newborns in Taleghani Hospital, Gorgan, Iran. *J Gorgan Uni Med Sci.* 2009; 11(2): 51-4.
- 2) Wheatley CM, Dickinson JL, Mackey DA, Craig JE, Sale MM. Retinopathy of prematurity: recent advances in our understanding. *Br J Ophthalmol.* 2002; 86(6): 696-700. doi: 10.1016/j.earlhumdev.2007.11.009. PMID: 12034695, PMCID: PMC1771164.
- 3) International Committee for the Classification of Retinopathy of Prematurity. The international classification of retinopathy of prematurity revisited. *Arch Ophthalmol.* 2005; 123(7): 991-9. doi: 10.1001/archophth.123.7.991. PMID: 16009843.
- 4) Stoltz Sjöström E, Lundgren P, Öhlund I, Holmström G, Hellström A, Domellöf M. Low energy intake during the first 4 weeks of life increases the risk for severe retinopathy of prematurity in extremely preterm infants. *Arch Dis Child Fetal Neonatal Ed.* 2016; 101(2): 108-13. doi: 10.1136/archdischild-2014-306816. PMID: 25678632, PMCID: PMC4789715.
- 5) Shah VA, Yeo CL, Ling YL, Ho LY. Incidence, risk factors of retinopathy of prematurity among very low birth weight infants in Singapore. *Ann Acad Med Singapore.* 2005; 34(2): 169-78. PMID: 15827664.
- 6) Lundgren P, Wilde Å, Löfqvist C, Smith LE, Hård AL, Hellström A. Weight at first detection of retinopathy of prematurity predicts disease severity. *Br J Ophthalmol.* 2014; 98(11): 1565-9. doi: 10.1136/bjophthalmol-2014-304905. PMID: 24963022, PMCID: PMC4389626.
- 7) Chen J, Smith LE. Retinopathy of prematurity. *Angiogenesis.* 2007; 10(2): 133-40. doi: 10.1007/s10456-007-9066-0. PMID: 17332988.
- 8) Mintz-Hittner HA, Kennedy KA, Chuang AZ; BEAT-ROP Cooperative Group. Efficacy of intravitreal bevacizumab for stage 3+ retinopathy of prematurity. *N Engl J Med.* 2011; 364(7): 603-15. doi: 10.1056/NEJMoa1007374. PMID: 21323540, PMCID: PMC3119530.

- 9) Austeng D, Källén KB, Hellström A, Jakobsson PG, Johansson K, Tornqvist K, et al. Screening for retinopathy of prematurity in infants born before 27 weeks' gestation in Sweden. *Arch Ophthalmol*. 2011; 129(2): 167-72. doi: 10.1001/archophthalmol.2010.346. PMID: 21320961.
- 10) Hartnett ME, Penn JS. Mechanisms and management of retinopathy of prematurity. *N Engl J Med*. 2012; 367(26): 2515-26. doi: 10.1056/NEJMra1208129. PMID: 23268666, PMCID: PMC3695731.
- 11) Darlow BA. Retinopathy of prematurity: new developments bring concern and hope. *J Paediatr Child Health*. 2015; 51(8): 765-70. doi: 10.1111/jpc.12860. PMID: 25757043.
- 12) Kemper AR, Wade KC, Hornik CP, Ying GS, Baumritter A, Quinn GE; Telemedicine Approaches to Evaluating Acute-phase Retinopathy of Prematurity (e-ROP) Study Cooperative Group. Retinopathy of prematurity risk prediction for infants with birth weight less than 1251 grams. *J Pediatr*. 2015; 166(2): 257-61. doi: 10.1016/j.jpeds.2014.09.069. PMID: 25449219, PMCID: PMC4308554.
- 13) Binkhathlan AA, Almahmoud LA, Saleh MJ, Srungeri S. Retinopathy of prematurity in Saudi Arabia: incidence, risk factors, and the applicability of current screening criteria. *Br J Ophthalmol*. 2008; 92(2): 167-9. doi: 10.1136/bjo.2007.126508. PMID: 18227198.
- 14) Rasolabadi M, Khaledi S, Khayati F, Kalhor MM, Penjvini S, Gharib A. Scientific production of Medical Universities in the West of Iran: A scientometric analysis. *Acta Informatica Medica*. 2015; 23(4): 206-9. doi: 10.5455/aim.2015.23.206-209. PMID: 26483592, PMCID: PMC4584087.
- 15) Kavurt S, Özcan B, Aydemir O, Bas AY, Demirel N. Risk of retinopathy of prematurity in small for gestational age premature infants. *Indian Pediatr*. 2014; 51(10): 804-6. PMID: 25362011.
- 16) Ghaseminejad A, Niknafs P. Distribution of retinopathy of prematurity and its risk factors. *Iran J Pediatr*. 2011; 21(2): 209-14. PMID: 23056789, PMCID: PMC3446155.
- 17) Abrishami M, Maemori GA, Boskabadi H, Yaeghobi Z, Mafi-Nejad S, Abrishami M. Incidence and Risk Factors of Retinopathy of Prematurity in Mashhad, Northeast Iran. *Iran Red Crescent Med J*. 2013; 15(3): 229-33. doi: 10.5812/ircmj.4513. PMID: 23984003, PMCID: PMC3745752.
- 18) Fayazi A, Heydarzadeh M, Feyz EH, Golzar A, Sadeghi K. Prevalence of Retinopathy of Prematurity in Preterm Infant Hospitalized in Tabriz Alzahra Hospital's NICU. *Medical journal of tabriz university of medical sciences*. 2009; 30(4): 63-6. doi: 10.5681/jcs.2012.013.
- 19) Enomoto H, Miki A, Matsumiya W, Honda S. Evaluation of oxygen supplementation status as a risk factor associated with the development of severe retinopathy of prematurity. *Ophthalmologica*. 2015; 234(3): 135-8. doi: 10.1159/000433565. PMID: 26112392.
- 20) Chen Y, Xun D, Wang YC, Wang B, Geng SH, Chen H, et al. Incidence and Risk Factors of Retinopathy of Prematurity in Two Neonatal Intensive Care Units in North and South China. *Chin Med J (Engl)*. 2015; 128(7): 914-8. doi: 10.4103/0366-6999.154294. PMID: 25836612, PMCID: PMC4834008.
- 21) Ortega-Molina JM, Anaya-Alaminos R, Uberos-Fernández J, Solans-Pérez de Larraya A, Chaves-Samaniego MJ, Salgado-Miranda A, et al. Genetic and environmental influences on retinopathy of prematurity. *Mediators of inflammation*. 2015; 2015: 764159. doi: 10.1155/2015/764159. PMID: 26089603, PMCID: PMC4454750.