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ORIGINAL ARTICLE

Prevalence and related factors of retinopathy of prematurity (ROP) in preterm infants in ophthalmology clinic of Birjand University of Medical Science from 2014 to 2016

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Abstract

Introduction: The prevalence of retinopathy of prematurity is expected to increase along with the developing of premature infants' care and better prognosis of these infants. The aim of this study was to evaluate the prevalence of retinopathy of prematurity in preterm infants.

Methods: According to this cross-sectional study, one same ophthalmologist examined the eyes of all the babies at 4 weeks postnatally or 32 weeks post-conceptional age, whichever was earlier, for all premature infants under 37 weeks and those who had ROP risk factor. These infants were referred to the ophthalmology clinic of Vali-asr Hospital by neonatologists and pediatricians. History and risk factor was assessed by the neonatologist on admission time. Data were analyzed with SPSS software (version 19) using Chi-square, and Fisher's Exact Test. The significance level was considered $P < 0.05$.

Results: A total of 209 patients were referred to the ophthalmologic clinic of Vali-asr hospital of whom 15 infants (7.2%) were diagnosed with retinopathy of prematurity. The prevalence of retinopathy of prematurity had a significant relationship with gestational age and birth weight. However, there were no significant associations with other risk factors (gender, oxygen, respiratory distress, sepsis, and phototherapy).

Conclusions: Overall, the prevalence of retinopathy of prematurity in our study was lower than that of other studies. Excellence in pre- and neonatal care, screening and early treatment of retinopathy of prematurity are keys to preventing vision loss induced by this disease. It is mandatory to ensure that these newborns have regular ophthalmologic support.

Key Words: Retinopathy of Prematurity; Infant; Premature; Risk Factors; Prevalence

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Introduction

Retinopathy of prematurity (ROP), a vascular retinopathy, develops only in the incompletely vascularized retinas of premature infants, leading to a wide range of outcomes from normal vision to blindness (1).

ROP was first described more than 60 years ago as *retrolental fibroplasia*. The introduction of closed incubators with the use of high levels of supplemental oxygen caused inhibition of the growth of retinal vessels in premature infants, eventually resulting in a complete retinal detachment behind the lens. Supplemental oxygen increased the risk of blindness but also improved survival. When oxygen use was curtailed in the 1950s, ROP incidence decreased but mortality and morbidity increased. Optimal oxygenation saturation levels balancing ROP risk against improved survival are still unknown (2). ROP has been reported to have two epidemics in the past in the developed countries. The first epidemic occurred in 1940-1950s and unmonitored supplemental oxygen was the principal risk factor. The second epidemic occurred during 1970-1980s despite careful monitoring of oxygen delivery to neonates. It was concluded that this epidemic was due to increased survival of VLBW babies (3, 4).

Worldwide, approximately 10% of births occur as preterm (before 37 completed weeks' gestational age). In countries with advanced neonatal intensive care units (NICU) care, most cases of ROP now occur among extremely low gestational age newborns (born <28 weeks' gestational age). Determining the current incidence of ROP in population-based studies, even among more developed countries, is challenging because there is considerable variability in study design, in gestational age of included premature infants, and in survival rates. Taken as a whole, reports suggest that there has not been a significant change in ROP incidence over time, perhaps explained by an increase in survival rates among very immature infants at high risk for ROP balanced against improved NICU care, which lowers ROP risk (2). ROP is becoming a significant problem in developing countries and these countries are experiencing the 3rd epidemic due to an increased rate of preterm deliveries and NICU facility for these babies. However, the lack of adequate resources and expertise to monitor blood gases and other variables is ultimately leading to increased ROP in these preterm babies (3, 4). Vision 2020 is a global initiative of the international agency for prevention of blindness where the mission is to eliminate avoidable blindness by 2020 (3, 6).

Because our NICU with update management started 6 years ago, we need to know about ROP outcomes of the admitted infants. The purpose of this study was to know the prevalence and to find maternal and neonatal risk factors for ROP in premature infants in the Birjand-based Vali-asr Hospital.

Methods

This cross-sectional study was conducted in the ophthalmology clinic of ROP, Department of Ophthalmology, Vali-asr Hospital of Birjand, in collaboration with Department of Pediatrics, NICU ward, on infants with gestational age less than or equal to 37 weeks from September 2014 to March 2016.

The ethics committee of Birjand University of Medical Sciences, Birjand, Iran, approved the study (approval code: IR.BUMS.REC.1394.284).

After the approval of the research design, we enrolled 206 infants in our study. All infants had been referred to the ROP clinic from Vali-asr Hospital NICU ward by a neonatologist.

On admission time in the NICU, the infants were weighed; their gestational age was assessed; and other clinical information was recorded including gender, mode of delivery, neonatal risk factors, i.e., RDS, sepsis, hyperbilirubinemia, any use and duration of supplemental oxygen, phototherapy, maternal history of gestational diabetes, drug abuse during pregnancy and abortion history.

Complete eye examination of all the babies was performed by the same ophthalmologist at 4 weeks postnatally or 32 weeks post-conceptional age, whichever was earlier. Pupillary dilatation was achieved with a mixture of 2.5% phenylephrine and 0.5% tropicamide instilled 3 times before the scheduled examination. Topical anesthetic 2% proparacaine was used. The examination was done using an indirect ophthalmoscope with 20 D lens or 28 D lens. The retinal findings were recorded as per guidelines of ICROP. Follow-up examinations were conducted until full vascularization of retina reached zone 3 or until full remission of ROP after laser treatment.

Data were analyzed using SPSS statistical package version 19. The prevalence of ROP was calculated in simple proportion. By using the chi-squared test and Fisher exact test. A probability (p) of less than 0.05 was considered significant.

Results

This study was conducted in the Department of Pediatrics in collaboration with the Department of Ophthalmology both affiliated with Birjand University of Medical Sciences. Out of the 209 babies enrolled, 15 babies were found to have ROP of whom 6 babies required treatment. The prevalence of ROP in this study was 7.2%.

A total of 111 cases (53.1%) were male and 98 cases were female. The mean gestational age was 31.46 ± 3.3 weeks; the minimum gestational age was 23 weeks and the maximum was 36 weeks plus 6 days. Weight average was 1652±60 grams ranging from 600 to 3799 grams and 48.3% of the cases (101 cases) were less than 1500 grams. Also, 51.7% (108) of cases were more than 1500 grams. A total of 143 infants had a history of fewer than 15 days oxygen therapy (68.4%); 122 infants had respiratory distress syndrome (58.4%); 33 infants had a history of sepsis (15.8%), and 137 infants had a history of phototherapy during admission (65.6%)(Table 1).

The average age of mothers was 28.56 years ranging from 17 to 45 years old. A total of 48 mothers (23%) had a history of abortions and 10 mothers (8.4%) had a history of drug abuse, Six cases (3.4%) had a history of diabetes and 8 mothers (3.4%) had a history of premature labor.

We could not find any significant relationship between the incidence of ROP and maternal risk factors including maternal age (p=0.43), maternal diabetes (p=0.64), maternal drug abuse (p=0.47), and history of abortion (p=0.46).

The study did not show any significant relationship between the prevalence of ROP and infants risk factors including sex (p=0.21), oxygen therapy (p=0.73), RDS (p=0.44), phototherapy (p=0.42), and sepsis (p=0.28). Nonetheless, we found significant relationships between the prevalence of ROP, gestational age (p=0.02) and birth weight (Table 2).

Table 1: Neonatal risk factors distribution

Variable	Groups	N (%)
Neonatal sex	Male	111(53.1)
	Female	98 (46.9)
Neonatal weight	>1500 gm	101 (48.3)
	<1500 gm	108 (51.7)
Oxygen consumption	Without	14 (6.7)
	>15 day	143 (68.4)
	<15 day	52 (29.4)
Respiratory distress	Positive	122 (58.4)
	Negative	87 (41.6)
Sepsis	Positive	33 (15.8)
	Negative	176 (84.2)
Phototherapy	Positive	137 (65.6)
	Negative	72 (34.4)

Table 2: Premature retinopathy comparative to neonatal risk factors

Variables	Groups	Retinopathy of prematurity		Total	P-value
		Yes	No		
Neonatal sex	**Male**	6 (5.4%)	105 (94.6%)	111 (100%)	0.21
	Female	9 (9.2%)	89 (90.8%)	98 (100%)	
Birth weight	**1500>**	12 (11.9%)	89 (88.1%)	101 (100%)	0.011
	1500<	3 (2.8%)	105 (97.2%)	108 (100%)	
Gestational age	**32>**	13 (10.2%)	114 (89.8%)	127 (100%)	0.02
	32<	2 (2.4%)	80 (97.6%)	82 (100%)	
Oxygen consumption	**NO**	0 (0%)	14 (100%)	14 (100%)	0.73
	15>	12 (8.4%)	131 (91.6%)	143 (100%)	
	15<	3 (5.8%)	49 (94.2%)	52 (100%)	
Respiratory distress	**Yes**	8 (6.6%)	114 (93.4%)	122 (100%)	0.44
	NO	7 (8%)	80 (92%)	87 (100%)	
Sepsis	**yes**	1 (3%)	32 (97%)	33 (100%)	0.28
	No	14 (8%)	162 (92%)	176 (100%)	
Phototherapy	**Yes**	9 (6.6%)	128 (93.4%)	137 (100%)	0.42
	No	6 (8.3%)	66 (91.7%)	72 (100%)	

Table 3: Prevalence of premature retinopathy in comparison to mother diseases

Variables	Groups	ROP		Total	P-value
		No	Yes		
Abortion	Yes	4 (8.3%)	44 (91.7%)	48 (100%)	0.46
	No	11 (6.8)	150 (93.2%)	161 (100%)	
Drug consumption	Yes	0 (0%)	10 (100%)	10 (100%)	0.47
	No	15 (7.5%)	184 (92.5%)	199 (100%)	
Diabetes	Yes	0 (0%)	6 (100%)	6 (100%)	0.64
	No	15 (7.4%)	188 (92.6%)	203 (100%)	

Discussion

ROP is a vasoproliferative disorder and among the preventable causes of blindness in children. As it is preventable, policies are required to manage it and thereby change the quality of life of premature infants.

We enrolled 209 babies admitted to NICU with the gestational age of ≤ 37 weeks. Out of these, 15 babies were found to have ROP, 6 of whom required treatment and the rest underwent spontaneous regression. In our study, there were some limitations. Our results may be different because we have included all preterm infants, whereas other articles have evaluated infants with weights lower than 1500 grams. Pannu M and et al. found the incidence of ROP in their ward as 40.3%. Nonetheless, their cases were infants less than 32 weeks and because there is a relationship between ROP and gestational age, these results are expected (4). Also, Larsson et al. found the incidence of ROP in infants less than 1500 grams on a prospective population-based study on the incidence of ROP in the Stockholm region in Sweden as 36.4% (7). Both of these studies show age and weight can change results. Another city in Iran had an incidence rate of ROP greater than that of our study and we think there is not a relationship between incidence and better care in Birjand. We believe it should be related to weight and age of our cases.

In our study, infants with ages lower than 30 weeks and weight less than 1000 grams were fewer than other studies. The age and weight means in our study are greater than in Karkhaneh et al's study. Accordingly, the incidence in their study is 34.5% that is higher than the rate in our study (8). The study of Mikaniki et al confirmed our opinion showing that the incidence of ROP was 47.3% for infants with gestational age ≤ 32 weeks. All 33 infants with ROP had a gestational age of ≤ 34 weeks. The incidence of ROP was 33.3% for infants with BW < 1500 grams. ROP developed in 2 (6%) infants with BW > 2000 grams (9) and a study in the southwestern region of Iran showed that the incidence rate of ROP is higher than that of other parts of the world (10, 11). All these studies show that our incidence is not comparable with other studies because of birth weight and gestational age. Of course, Saeidi et al had ROP incidence near to us and that is 8.5%. The number of cases in their study is considerably lower than that of ours totaling only 55 cases (12).

Our study just found a significant relationship between the incidence of ROP, gestational age and birth weight. We could not find any relationship between ROP incidence and respiratory distress syndrome, sepsis, phototherapy, and oxygen consumption. This can be due to the same issue, average of gestational age and weight in our study. Saedi and colleague reported the same results, whereas other studies are different (12). For example, Gaseminejad and colleague could not find any associations between ROP, birth weight and gestational age. (13) and other studies found a relationship between oxygen therapy and ROP (14, 15). Coutinho et al found significant relationships between ROP, sepsis, and persistence of ductus arteriosus, respiratory distress syndrome, and oxygen therapy; however, we could not (16).

Conclusions

The pathogenesis of ROP is multifactorial. In this study, we were able only to discover the relationship between these two issues (i.e., birth weight and gestational age) and ROP. Certainly, further research is needed to find other risk factors.

The prevalence of ROP was 7.2%. Overall, the prevalence of ROP in our study was lower than other studies. We think one of the most important reasons for this result is less incidence of

extremely low birth weight in our study in comparison to other studies. Of course, this needs more investigation to confirm our hypothesis.

Six infants who needed treatment for ROP were referred to the advanced ward. ROP remains a major complication in premature newborns despite all the advances that have been made in recent years. Excellence in pre- and neonatal care, screening and early treatment of ROP are keys to preventing vision loss induced by this disease. It is mandatory to ensure that these newborns have regular ophthalmologic support.

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Conflict of Interest

The authors declare that they have no conflict of interest.

References

1. Dale P. Retinopathy of Prematurity. In: Martin R, Fanaroff A, Walsh A (eds). neonatal-perinatal medicine. 8th ed. London: Mosby; 2006.

2. Sun Y, Hellstrom A, Smith L. Retinopathy Of Prematurity. In: Martin R, Fanaroff A, Walsh A (eds). Fanaroff and martin's neonatal-perinatal medicine diseases of the fetus and infant. 10th ed. Philadelphia: Elsevier;2015. pp: 1768-74.

3. Gilbert C. Retinopathy of Prematurity: A global perspective of the epidemics, population of babies at risk and implications for control. Early Hum Dev. 2008;84(2):77-82. doi: 10.1016/j.earlhumdev.2007.11.009.

4. Pannu M, Kumar A, Singh R, Singh K, Dhillon S, Singh S. Incidence and Risk factors for Retinopathy of Prematurity in Neonates of weight <1.5 kg and/ or <32 weeks of Gestation in a tertiary care Hospital. Int J Curr Res Med Sci. 2017;3(7):75-82. DOI: http://dx.doi.org/10.22192/ijcrms.2017.03.07.013.

5. Gilbert C, Rahi J, Eckstein M, O'Sullivan J, Foster A. Retinopathy of prematurity in middle-income countries. Lancet. 1997; 350(9070):12-4. DOI: 10.1016/S0140-6736(97)01107-0.

6. Gilbert C, Foster A. Childhood blindness in the context of vision 2020 – the right to sight. Bull World Health Organ. 2001;79(3):227-32.

7. Larsson E, Carle-Petrelius B, Cernerud G, Ots L, Wallin A, Holmström G. Incidence of ROP in two consecutive Swedish population-based studies. Br J Ophthalmol. 2002;86(10):1122-6.

8. Karkhaneh R, Mousavi SZ, Riazi-Esfahani M, Ebrahimzadeh SA, Roohipoor R, Kadivar M, et al. Incidence and risk factors of retinopathy of prematurity in a tertiary eye hospital in Tehran. Br J Ophthalmol. 2008;92(11):1446-9. doi: 10.1136/bjo.2008.145136.

9. Mikaniki E, Rasolinejad S, Mikaniki M. Incidence and risk factors of retinopathy of prematurity in Babol, North of Iran. Ophthalmic Epidemiol. 2010; 17(3):166-70. doi: 10.3109/09286581003734860.

10. Feghhi M, Altayeb SMH, Haghi F, Kasiri A, Farahi F, Dehdashtyan M, et al. Incidence of Retinopathy of Prematurity and Risk Factors in the South-Western Region of Iran. Middle East Afr J Ophthalmol. 2012;19(1):101-6. doi: 10.4103/0974-9233.92124.

11. Edy Siswanto J, Sauer PJ. Retinopathy of prematurity in Indonesia: Incidence and risk factors. J Neonatal Perinatal Med. 2017;10(1):85-90. doi: 10.3233/NPM-915142.

12. Saeidi R, Hashemzadeh A, Ahmadi S, Rahmani S. Prevalence and Predisposing Factors of Retinopathy of Prematurity in Very Low birth weight Infants Discharged from NICU. Iran J Pediatr. 2009;19(1):59-63.

13. Ghaseminejad A, Niknafs P. Distribution of Retinopathy of Prematurity and Its Risk Factors. Iran J Pediatr. 2011;21(2):209-14.

14. Colaizy T, Longmuir S, Gertsch K, Abràmoff MD, Klein JM. Use of a Supplemental Oxygen Protocol to Suppress Progression of Retinopathy of Prematurity. Invest Ophthalmol Vis Sci. 2017 Feb 1;58(2):887-891. doi: 10.1167/iovs.16-20822.

15. Reyes ZS, Al-Mulaabed SW, Bataclan F, Montemayor C, Ganesh A, Al-Zuhaibi S, et al. Retinopathy of prematurity: Revisiting incidence and risk factors from Oman compared to other countries. Oman J Ophthalmol. 2017;10(1):26-32. doi: 10.4103/ojo.OJO_234_2014.

16. Coutinho I, Pedrosa C, Mota M, Azeredo-Lopes S, Santos C, Pires G, et al. Retinopathy of prematurity: results from 10 years in a single neonatal intensive care unit. J Pediatr Neonat Individual Med. 2017;6(1):e060122.