Original Article

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Distribution of Retinopathy of Prematurity and Its Risk Factors

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Abstract

Objective: This study was conducted to determine the distribution and risk factors of retinopathy of prematurity (ROP) in premature infants referred to neonates intensive care unit (NICU) of central hospital of Kerman University of Medical Sciences, to obtain primary information on ROP in Kerman, Iran.

Methods: In a cross sectional prospective study, data of premature infants screened for ROP including possible risk factors and eye examination results were recorded during 2006-2008 and analyzed by using logistic regression and chi-square tests.

Findings: Out of 83 premature infants, 24 (29%) had different stages of ROP (CI 95%: 0.19-0.39). The infants' mean gestational age (GA) and mean birth weight (BW) in ROP group were 30.17±1.8 weeks and 1247.92±237.1 grams (g), respectively. Logistic regression analysis showed a significant relation between GA and BW with ROP (P<0.001). Indication for treatment was set in 6 (25%) infants.

Conclusion: The results of this study illustrate a relatively high prevalence of ROP in this series. GA and BW were independent ROP determinants.

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Key Words: Prematurity; Prevalence; Retinopathy; Birth Weight; Gestational Age; Neonate

Introduction

Retinopathy of prematurity (ROP) is still one of the important causes of blindness in premature infants. ROP forms during retinal vessels development and affects only premature infants whose retinal vessels are not fully formed[1,2].

In the United States about 300 infants out of every one million lose at least one of their eyes secondary to ROP[3]. ROP is rare in infants born with more than 2000g weight[4]. Risk of ROP increases with reduction of gestational age (GA) and body weight (BW). Oxygen is not the unique risk agent of the disease and different factors are involved in a complex way[5]. It is suggested that decreased oxygen usage in neonates can lessen the incidence and severity of this complication[6,7]. Nowadays, other various factors rather than this,

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are identified as ROP etiology[8]. Risk factors known for this disease include low GA, low BW, oxygen therapy, sex, phototherapy, intra-ventricular hemorrhage (IVH) and blood transfusion[5,6,7,9-13].

In countries with low socio-economic status incidence of ROP is much less, due to low survival of premature infants[14]. Risk factors may be different in Iran. Improvement of neonatal care in this country has increased survival rate of premature infants and as a result, increased incidence of ROP. Clarifying the incidence of disease in different parts of the country seems to be necessary. There is no information about characteristics of ROP in Kerman.

Regarding GA and BW, we need screening criteria for ophthalmic examination of premature infants. Kerman is one of the deprived and developing provinces located in south-east Iran, and this is the first study carried out on ROP in this area.

Subjects and Methods

This was a descriptive cross sectional prospective study. All premature infants in neonates intensive care unit (NICU) of Kerman University of Medical Sciences with criteria of GA of 36 weeks or less and BW of 2500g or less were referred for ophthalmic examination 4-6 weeks after birth, during November 2006 to December 2008. We chose the patients by easy sampling method. As we have no screening criteria for ROP in Iran, we did not exclude any infants of less than 36 weeks gestation and 2500g BW, which is different from most international guidelines.

Our NICU has 26 beds and is approved for training of fellows in neonatology, and related to a tertiary center including prenatal and postnatal wards. Average number of admitted babies in this NICU is about 90 per month, 70 percent of whom are premature infants. All information related to GA, BW, sex, existence of respiratory distress syndrome (RDS), oxygen therapy, blood trans-fusion, phototherapy, sepsis and IVH were recorded by researchers in a check list. All infants were examined for the presence of ROP by an ophthalmologist.

Staging of disease was recorded according to international classification of ROP[15]. Based on finding in primary examination, the next visit was set for 1 to 3 weeks later, and continued until development of complete retinal vascularization without signs of ROP or regression of ROP[16]. In cases with signs of threshold ROP, treatment started as soon as possible[16].

To compare the GA, BW, infant's age at examination and oxygen therapy in two groups, t-test was used. Chi square test was used to compare categorical and qualitative variables (such as sepsis, oxygen therapy, acidosis, etc) in both groups. Logistic regression statistic tests were used for acquiring Odds ratio (OR) in order to specify ROP likelihood in study groups. Ethics committee of Kerman University of Medical Sciences approved this study.

All analyses were performed using SPSS 15.0 and $P<0.05$ was considered as statistically significant.

Findings

During the study period, 91 premature infants were referred for eye examination and in 83 cases follow-up study were completed. Forty nine (59%) patients were males. ROP was seen in 24 (29%) infants (CI 95%: 0.19-0.39).

As shown in Table 1, ROP and no ROP groups have significant difference concerning mean GA, mean BW and mean time of oxygen therapy and hypoglycemia. This means that infants with ROP had less GA and BW than no ROP patients. Also, patients with ROP had higher rate of oxygen therapy. Regarding other variables such as existence of other syndromes, blood transfusion, phototherapy, sepsis, IVH and acidosis there was no statistically significant difference between the two groups.

Table 2 shows that 91.7% infants with ROP had GA of 32 weeks or less. The difference between ROP and no ROP group was significant and in GA<32 weeks it was more than that in GA>32 weeks ($P=0.006$).

BW distribution in the two groups is compared in Table 3. It shows that about 80% of infants in

Table 1: Comparison of patients in ROP and no ROP groups concerning basic variables

Variables	ROP	No ROP	*P* value
Gestational age (weeks) [Mean (SD)]	30.2 (1.8)	32.4 (1.6)	<0.001
Birth weight (gr) [Mean (SD)]	1247.9 (237.1)	1663.6 (335.0)	<0.001
Infantile age (days) at first eye exam [Mean (SD)]	46.1 (10.8)	43.3 (11.0)	0.3
Duration of oxygen therapy (hours) [Mean (SD)]	396.9 (235.6)	155.7 (231.8)	0.005
Existence of other syndromes (Frequency)	13/24 (54.1%)	37/59 (62.7%)	0.5
Respiratory distress syndrome (Frequency)	9/24 (37.5%)	31/59 (52.5%)	0.2
Oxygen therapy (Frequency)	22/24 (91.6%)	57/59 (96.6%)	0.3
Blood Transfusion(Frequency)	3/24 (12.5%)	4/59 (6.7%)	0.4
Phototherapy (Frequency)	18/24 (75%)	43/59 (72.8%)	0.8
Sepsis (Frequency)	3/24 (12.5%)	4/59 (6.7%)	0.4
Intraventricular hemorrhage (Frequency)	3/24 (12.5%)	4/59 (6.7%)	0.4
Hypoglycemia (Frequency)	4/24 (16.6%)	2/59 (3.3%)	0.03
Acidosis (Frequency)	3/24 (12.5%)	4/59 (6.7%)	0.4

ROP: Retinopathy of prematurity

ROP group had BW of 1500g or less, and no ROP was seen in infants with 2000g or more.

Logistic regression results are shown in Table 4 for all independent variables. GA of 32 weeks or less had significant relationship with ROP. Also it was shown that the chance of ROP in infants with BW of less than 1000 g, was 20.5 times more than in infants with 1500g or more.

A number of 6 (25%) out of 24 ROP patients had indication for treatment. 3 patients underwent laser therapy in both eyes, in 2 cases both eyes were cured, and in 1 case one eye was cured and in the other eye macular dragging developed. 2 cases underwent deep vitrectomy in both eyes. In one of them both eyes became blind and in one case one eye cured and one eye became blind. One infant was untreatable due to disease progression in both eyes in the first visit.

Mean GA and BW in infants who had indication for treatment were 29.5 weeks and 1050 g respectively.

Discussion

ROP is one of the main reasons of blindness in infants, which in many cases is predictable and curable[9]. Increased survival of premature infants has led to a higher incidence of ROP in our region and we need more information about the risk factors of the disease. Our study is the first study carried out on ROP in Kerman (Iran). ROP is seen in 29% of premature infants referred to mentioned center in Kerman.

In Cryotherapy ROP multicenter study in the United States, signs of ROP were seen in 66% of infants with a BW of less then 1251g and in 82% of those with a BW of less than 1000 g[16].

The incidence of ROP among infants born in Tehran was 26.5% and in the whole study (including patients referred from other cities) was 34.5%, reported by Karkhaneh et al, in 2008[17]. ROP incidence shows some differences in Kerman in comparison with Tehran. For example, ROP

Table 2: Gestational age of infants in ROP and no ROP groups

Gestational age	ROP (%)	No ROP (%)	*Chi²*	*P* value
>32 weeks	2 (8.3%)	23 (39 %)	7.61	0.006
≤32 weeks	22 (91.7%)	36 (61%)		
Total	24 (29%)	59 (71%)	--	--

ROP: Retinopathy of prematurity

Table 3: Birth weight of infants in the two groups

Birth Weight (BW)	ROP (%)	No ROP (%)
≤1000	5 (20.8%)	2 (3.4%)
1000<BW≤1250	9 (37.5%)	6 (10.2%)
1250<BW≤1500	5 (20.8%)	10 (16.9%)
1500<BW≤2000	5 (20.8%)	31 (52.5%)
>2000 g	0 (0%)	10 (16.9%)

ROP: Retinopathy of prematurity/ χ^2=21.37; *P*-value<0.001

incidence was 27.7% in infants with 2000 g weight or less in Tehran, but it was 32% in infants with the same weight in Kerman. Also, ROP incidence was 40.8% in infants with less than 1500 g in Tehran, while it was 51% in infants with the same weight in Kerman. Furthermore, ROP incidence was 49.4% in infants with 1000 g or less in Tehran, while it was 71% in infants with the same weight in Kerman[17].

In our study, infant's BW and GA had a significant relationship with ROP prevalence, so none of the infants with more than 1800 g BW and 33 weeks GA had ROP. These results are compatible with some other studies[18-20].

Unlike Karkhaneh study in Tehran[17] and some other studies such as Weinberger study in USA[21], Rudank in Finland[22], Kim in Japan[23] and Lin in China[24], no significant relationship was observed between oxygen therapy and ROP prevalence in our study. The reason is that, all infants in ROP and no ROP groups in our study were referred from NICU and most of them had history of oxygen therapy in that ward.

Palmer et al[25] and Khatami et al[26] reported that duration of oxygen therapy is more determinative in incidence of ROP than oxygen therapy alone, also according to Bayat-Mokhtari et al study[27] duration of oxygen therapy is one of main risk factors for development of threshold ROP, which are compatible with our study in which relation of mean time of oxygen therapy and prevalence of ROP was statistically significant (*P*=0.005).

Lucey and Dongmon[28] have reported that, although oxygen therapy is effective in ROP incidence, other factors such as low BW are more important. Saeidi et al[29] reported that low GA,sepsis and respiratory distress syndrome were independent preditorsfor the development of ROP.

ROP incidence varies in different cities and

Table 4: Logistic regression results for risk factors of Retinopathy of prematurity

Potential risk factors		Odds ratio (95% CI)	*P* value
Gestational age	**>32 weeks**	1	0.013
	≤32 weeks	7.02 (1.5- 32.7)	
Birth Weight (BW)	**>1500 g**	1	
	1250<BW≤1500	4.8 (1.05- 19.95)	0.04
	1000<BW≤1250	12.3 (3.06 – 49.32)	0.001
	≤1000	20.50 (3.11 - 134.94)	0.002
Existence of other syndrome		0.93 (0.34- 2.52)	0.9
Respiratory distress syndrome		0.66 (0.24- 1.79)	0.4
Blood Transfusion		1.89 (0.38- 9.27)	0.4
Phototherapy		0.94 (0.25- 3.45)	0.9
Sepsis		1.89 (0.38- 9.27)	0.4
Intraventricular hemorrhage		1.89 (0.38- 9.27)	0.4
Hypoglycemia		5.55 (0.93- 32.97)	0.06
Acidosis		1.89 (0.38- 9.27)	0.4

countries that can be secondary to differences in facilities and equipments which can provide survival possibility of premature infants.

According to our study, 25% of ROP cases had indication for treatment. None of babies who needed treatment had GA more than 30 weeks and BW more than 1300 g. On the other hand, all infants whose treatment was not successful and led to blindness did not come for eye examination on predetermined time due to individual cultural and economical problems.

We studied only the infants referred from NICU, and some premature infants were not admitted to NICU at all. As a result our study population does not show the real population. So, it seems that this prevalence may not be the real distribution of ROP in Kerman. Infant's mortality with very low BW and GA could cause missing of some ROP cases.

Conclusion

Our study shows a relatively high rate of ROP. We need guidelines for ROP screening for infants in Iran. Knowledge about the disease should be increased particularly in parents of premature infants with emphasis on importance of accurate time of eye examination. To remove some limitations of this study we suggest similar studies with greater sample size including premature infants not staying in NICUs.

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Conflict of Interest: None

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