



# The Open Ophthalmology Journal

Content list available at: [www.benthamopen.com/TOOPHTJ/](http://www.benthamopen.com/TOOPHTJ/)

DOI: 10.2174/1874364101610010017



## Retinopathy of Prematurity in Neonates and its Risk Factors: A Seven Year Study in Northern Iran

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### Abstract:

#### Purpose:

An important cause of avoidable childhood blindness is retinopathy of prematurity (ROP) in countries with high human development index and also in some emerging economies countries. To date, no research have been conducted on analyzing data of ROP prevalence in Babol, and this is the first research performed on ROP in this area.

#### Methods:

All VLBW babies who referred to Babol ophthalmology center over the seven years, from February 2007 to December 2013 were enrolled in this descriptive cross-sectional research. A team of researchers recorded patients' information completely in check lists. A single experienced ophthalmologist performed ophthalmologic examination of patients.

#### Result:

The incidence of ROP of any stage in Babol was determined to be 306 (45%) of all babies enrolled in this study. In present study, key risk factors of ROP were low gestational age, oxygen therapy more than five days and low birth weight.

#### Conclusion:

The findings of current study demonstrate that the main risk factors of developing ROP in newborns are multiple gestation, low birth weight, oxygen therapy for more than five day. Therefore, the progression of ROP to blindness will be prevented by a high index of suspicion, suitable screening, prompt diagnosis, and early treatment.

**Keywords:** Birth weight, multiple gestation, prevalence, retinopathy of Prematurity, risk factors, neonates.

## INTRODUCTION

Retinopathy of prematurity (ROP) affects immature vasculature of premature infants' eyes. This disease can appear in mild and aggressive forms. No visual sequelae is resulted in the mild form, while aggressive type is along with neovascularization and develop to retinal detachment and blindness [1, 2]. The prevalence of ROP has enhanced because of surviving smaller and younger infants [3].

In countries with high human development index and also in some emerging economies countries, this disease is a main avoidable cause of childhood blindness [4]. ROP is more prevalent in premature babies with low birth weight. Fielder reported the development of ROP in 51% of infants weighing less than 1700 g. Overall, the evidence of ROP is recognized for more than 50% of premature babies weighing less than 1250 gr at birth, and stage 3 ROP is observed in approximately 10% of these babies [5, 6].

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On average, 500-700 cases of blindness as a result of ROP are annually reported among American newborns. This can be stated as 30,000 life years of vision in terms of life years of blindness. 2100 newborns will annually be affected by cicatricial sequel such as myopia, blindness, strabismus, and late-onset retinal detachment [7 - 9]. The thumb rule is that several types of strabismus or refractive error will progress in about 20% of all premature newborns by 3 years of age [10]. For this reason, babies younger than 32 weeks or less than 1500 gr are given follow-up care every 6 months, regardless not or whether ROP is present [5, 11].

Low GA, low BW, sex, oxygen therapy, intra ventricular hemorrhage (IVH), phototherapy and blood transfusion are known as risk factors of this disease [12].

There has been no research until now to analyze data of ROP incidence in north of Iran. Accordingly, this is the first research conducted on ROP prevalence in Babol, which is one of the deprived and developing provinces in north Iran.

## MATERIALS AND METHODOLOGY

All very low birth weight (VLBW) babies referred to Babol ophthalmology center over the seven years from February 2007 to December 2013 were entered in this descriptive cross-sectional research. The study obtained ethics approval from the Ethics Committee of Babol University of Medical Sciences. Easy sampling method is used to select the patients in this study. Babies who died before a retinal examination were omitted from the study.

Unlike most international guidelines, newborns with a gestational age less than 36 weeks and 2500g birth weight (BW) were not omitted from the study as there is no screening criteria for ROP in Iran. All information corresponding to sex, gestational age (GA), birth weight, presence of respiratory distress syndrome (RDS), delivery type, oxygen therapy and sepsis were recorded by a team of scientists in a check list. A single experienced ophthalmologist performed ophthalmologic examination of patients.

T-test was applied to perform a comparison between two groups in the terms of the GA, BW, infant's age at examination and oxygen therapy. The comparison of categorical and qualitative variables including sepsis, oxygen therapy, etc. in groups was performed using chi-square test. In order to identify the probability of ROP in study groups, odds ratio (OR) was obtained by using logistic regression statistic tests. SPSS software (Version 21) was used to analysis all data. A P value < 0.05 was considered statistically significant.

## RESULT

During the study, 680 of 865 VLBW newborns who were referred were followed up for ROP development. 425 (62.5%) males and 255 (37.5%) females were involved in ROP group. Table 1 shows the average birth weight was  $1713.9 \pm 416.7$  grams and the average gestational age was  $31.45 \pm 2.21$  weeks (7% was 25-28 week, 55% was 29-32 week and 38% was more than 32 week).

The overall incidence of ROP in any stage was 306 (45%) among babies who referred to Babol ophthalmology center. Of 306 subjects, 52 (16.99%) subjects were in stage I of ROP, 193 (63.07%) subjects were in stage II and 61 (19.93%) subjects were in stage III or III<sup>+</sup>.

**Table 1. Demographic and perinatal characteristics of the study neonates.**

Characteristic	No (N %)
Sex	
Male	425 (62.5%)
Female	255(37.5%)
Mean birth weight (gr)	1713.9 ± 416.7
Birth weight(groups)	
500-1000	48(7%)
1001-1500	197(29%)
1501-2000	292(43%)
>2000	143(21%)
Gestational age	
25-28	48(7%)
29-32	374(55%)
>32	258(38%)
Delivery type	
NVD	201(29.5%)
CS	479(70.5%)

(Table 3) contd....

Characteristic	No (N %)
RDS Yes No	524(77%) 156(23%)
Sepsis Yes No	113(16.7%) 567(83.3%)
Mean duration of oxygen therapy (day)	5.21 ± 2.45

Table 2 shows the results of logistic regression for all independent variables. There was a significant relationship between GA of 32 weeks or less and ROP ( $P < 0.001$ ).

Furthermore, it was observed that babies with BW of less than 1500 g are 3.5 times more at risk for ROP compared to babies with 1500g or more. A significant relationship was observed between sepsis and ROP ( $P < 0.001$ ).

Table 2. Simple regression analysis results for ROP.

Characteristic		ROP N(%)	No ROP N(%)	OR	CI	P-Value
Sex	Male	211(69%)	214(57.2%)	0.787	0.034-1.78	0.50
	Female	95(31%)	160(42.8%)			
GA	<32W	141(46%)	71(19%)	2.913	1.237-6.862	0.01
	≥32w	165(54%)	303(81%)			
Oxygen therapy >5 day	Yes	267(87.2%)	245(65.5%)	1.793	0.629-5.110	0/32
	No	39(12.8%)	129(34.5%)			
RDS	Yes	141(46%)	183(49%)	0.853	0.380-1.913	0/87
	No	165(54%)	191(51%)			
Sepsis	Yes	65(21%)	41(10%)	2.889	1.093-7.633	0.04
	No	241(79%)	333(90%)			
Birth weight(gram)	<1500gr	133(43.5%)	83(22.1%)	3.512	1.415-8.719	0.007
	1500gr≤	173(56.5%)	291(77.9%)			
ROP stage	I	52(16.99%)	0(0%)	2.713	1.123-7.766	0.001
	II	193(63.07%)	0(0%)			
	III	61(19.93%)	0(0%)			

In ROP group, the mean oxygen therapy was  $7.12 \pm 4.32$  day and this value in healthy group was  $3.23 \pm 2.18$  day. Thus, there is no significant relationship between oxygen therapy with ROP ( $P > 0.05$ ).

## DISCUSSION

In current study, the incidence of ROP in any stage, from February 2007 to December 2013 was 306 (45%) among babies referred to Babol ophthalmology center. ROP is considered as an important avoidable cause of blindness in children in countries with high human development index and also in some emerging economies countries [4]. One country is different from another one in terms of the ROP prevalence depending on birth weights, gestational age, and risk factors. Three epidemics have been reported since 1942 after recognizing ROP: The first epidemic was during 1940-1945 when oxygen therapy was recognized as the main reason; the next one occurred between 1960-1970 due to developing neonatal care in industrial countries that enhanced survival of babies with ELBW; and the last one from 1980 until now because of increasing the survival of preterm babies with gestational age more than 32 weeks and a birth weight greater than 1500 grams using the newborn care accessible in developing countries with limited resources [13, 14].

The ROP rate in the current study was 45 %, which was higher as compared to available literature in this context including 32.4 % in Pakistan [15], 29.5 % in Tehran [16], 29.2 % in Singapore [18], 29 % in Kerman (southern Iran) [19], and 10.45 % in the United States [17]. Moreover, Sabzehi *et al.* [20] reported that the ROP incidence in Tehran was 17.4 % in 3 years study. In another study conducted by Mousavi *et al.* [21], the prevalence of ROP in Farabi hospital of Tehran was 34.4% in 4 years. Furthermore, the ROP prevalence was reported 37.1% by Mutlu *et al.* [22].

The outstanding risk factors for ROP have been addressed in this study; our findings are in a good accordance with those obtained from other studies. it was found that multiple gestations is an independent risk factor in progression of

ROP in studied subjects as well as the results of Blumenfield's study, although there was no difference between the ROP severity for children of a multiple gestation and infants of singletons [23]. In a research conducted by Riazi-Esfahani *et al.* [24], there was observed no significant difference in the rate or severity of ROP between babies of a multiple gestation and singletons unlike the study of Dos Santos Motta *et al.* [25] on 26 cases in which multiple gestation was considered as a risk factor for progression and severity of ROP.

It was found that oxygen therapy duration is an independent risk factor for ROP that was > 40 days, > 30 days, > seven days and > five days in the studied of Niwald *et al.* [26], Pinheiro *et al.* [27], Hakeem *et al.* [28] and present study, respectively.

## CONCLUSION

The findings of current study demonstrate that the main risk factors for infants to develop ROP are multiple gestation, low birth weight, oxygen therapy for more than five days. Therefore, the progressing ROP to blindness will be prevented with a high index of suspicion, apposite screening, rapid diagnosis, and early treatment.

## CONFLICT OF INTEREST

The authors confirm that this article content has no conflict of interest.

## ACKNOWLEDGEMENTS

Declared none.

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Received: March 29, 2015

Revised: June 17, 2015

Accepted: June 17, 2015

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