• Investigation •

Incidence and risk factors of retinopathy of prematurity and utility of the national screening criteria in a tertiary center in Iran

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Abstract

• AIM: To determine the incidence and risk factors of retinopathy of prematurity (ROP) and the sensitivity of current screening criteria in a tertiary eye center in Tehran, Iran.

• METHODS: In a cross-sectional observational study, neonates weighing ≤2000 grams at birth or born <34wk gestational age (GA) and all other infants at risk of ROP admitted to the neonatal intensive care unit (NICU) or referred to our ROP clinic were investigated. The incidence of ROP and severe ROP (*i.e.* patients needing treatment) were determined. The associations between risk factors and the development and severity of ROP were assessed. We also examined the sensitivity of the current national screening guideline in Iran.

• RESULTS: Among 207 infants, the incidence of ROP and severe ROP was 33.3% and 11.1%, respectively. Mean GA and birth weight (BW) were significantly lower in ROP *vs* non-ROP infants (29±2wk *vs* 33±3wk, *P*<0.001; 1274±489 g *vs* 1916±550 g, *P*<0.001, respectively). Univariate analysis displayed significant association between ROP incidence and GA, BW, NICU admission period, blood transfusion, surfactant usage, sepsis, intraventricular hemorrhage and patent ductus arteriosus (*P*<0.05 for all). BW [relative risk (RR): 0.857 (0.711-0.873), *P*<0.001], GA [RR: 0.788 (0.711-0.873), *P*<0.001] and blood transfusion [RR: 1.888 (0.995-3.583), *P*=0.052] were independent ROP risk factors. The sensitivity of country-specific screening guidelines was 95.7% and 100% for overall and severe ROP detection, respectively.

• CONCLUSION: ROP incidence is relatively high in Iran. Identifying ROP risk factors results in more accurate screening and reduces the risk of irreversible vision loss. The ROP screening criteria utilized in Iran are efficient at the present time.

• KEYWORDS: retinopathy of prematurity; incidence; risk factors; screening; Iran

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INTRODUCTION

Retinopathy of prematurity (ROP) in its advanced stages is a vasoproliferative retinal disease that affects premature infants[1]. Low gestational age (GA), low birth weight (BW) and high concentration oxygen therapy are the major ROP risk factors[2]. Regardless, some authors have reported ROP in cases without oxygen therapy[3-5]. In addition to the major risk factors, other factors such as anemia[6], insulin-like growth factor-1 (IGF-1)[7], mean platelet volume (MPV)[8], thrombocytopenia[9], bilirubin level, gender[10], multiple gestation[11], intraventricular hemorrhage (IVH)[12] and blood transfusion[13] were considered to be effective in incidence and progression of ROP.

According to the World Health Organization (WHO), ROP is an important cause of avoidable childhood blindness in developing countries[14]. A third epidemic of ROP has occurred in developing countries such as Iran[15]. The improvement of neonatal care in Iran has increased the survival rate of premature infants and consequently, the incidence of ROP.

However, there are few studies which have evaluated the incidence and risk factors of ROP in Iran[16-17]. Additionally, the ROP screening criteria in Iran was determined to be different from developed countries. The American Academy of Pediatrics (AAP) screening guidelines for ROP recommends screening for infants with BW≤1500 g or GA of ≤30wk[18]. It has been reported that these guidelines are inadequate for screening in less/moderately developed countries[19].

The aim of the current study was to determine the overall incidence of ROP and severe ROP at a tertiary eye care center, to investigate a wide range of risk factors regarding ROP development, and to test the sensitivity of Iranian screening criteria for ROP[20].

SUBJECTS AND METHODS

Ethical Approval The study was approved by the Ethics Committee of our institute (IRB code: Ir. Sbmu.msp.rec.1396.519) and performed in agreement with the ethical principles in the Declaration of Helsinki. Written informed consent was obtained from the parents.

This was a cross-sectional observational study performed from August 2016 through August 2017 at a tertiary eye care center. Preterm infants with BW≤2000 g or GA<34wk as well as selected infants with an unstable clinical course according to the determination of their pediatricians or neonatologists with BW>2000 g or GA≥34wk were included. The infants were examined first between 4 and 6wk after birth or within the 31st and 33rd weeks postmenstrual age, whichever occurred later. The stages and zones of ROP were determined according to the International Classification of ROP[21]. The examination was done biweekly or earlier based on disease severity, and continued until vascularization was complete or the disease progressed to Type 1 ROP based on early treatment for ROP (ET-ROP)[22]. The infants with Type 1 ROP or stage 4 or 5 of ROP were categorized as severe ROP and treated accordingly. Mild ROP was defined as ROP that did not meet the criteria for treatment[22].

Eye Examination Methods All examinations were done by four experienced retina specialists. Pupils were fully dilated using tropicamide 0.5% and phenylephrine 5% eye drops. After topical anesthesia, each infant was examined with an indirect ophthalmoscope using a lid speculum, a scleral depressor and a +20 D or +30 D lens.

Data Collection Infant information and risk factors were collected including delivery method (cesarean section versus vaginal delivery), GA, BW, gender, Apgar scores at 1min, hemoglobin and bilirubin levels, septicemia, IVH, MPV, platelet count, IGF-1 level, blood transfusion, neonatal intensive care unit (NICU) admission period (days), gestational diabetes mellitus (GDM), necrotizing enterocolitis (NEC), patent ductus arteriosus (PDA), acute respiratory distress syndrome (ARDS) and use of surfactant. Furthermore, maternal information was gathered including maternal age, multiple gestation pregnancies, history of pre-eclampsia, eclampsia and hemolysis, elevated liver enzyme levels, and low platelet levels (HELLP) syndrome. The results of fundus examination were also recorded (*i.e.* stage, zone, plus disease and necessity for therapy).

Statistical Analysis Data were analyzed using SPSS software (SPSS 24.0, SPSS Inc, Chicago, IL, USA). To describe data, we used mean, standard deviation, median, range, frequency and percentage. Simple log binomial regression was used to find the relative risk of different risk factors on incidence and severity of ROP. In addition, multiple log binomial regression was employed to compute the adjusted risk ratio as well as the simultaneous association of presumed risk factors and ROP incidence and severity. To assess the diagnostic power of the defined criteria, we used sensitivity, specificity, positive and negative predictive value as well as positive and negative likelihood ratio. All the estimated measures were accompanied by corresponding 95% confidence intervals (CI). We used the Poisson method to calculate the 95%CI of incidences. *P* value less than 0.05 was considered statistically significant.

RESULTS

In total, 216 infants were screened for ROP. Of them, 9 subjects were excluded due to incomplete data related to ROP exams. Therefore, the data of 207 infants were used for statistical analyses; 100 (48.3%) female and 107 (51.7%) male (Table 1). Of all cases, 91 (44.8%) received surfactant, 90 (43.9%) received blood transfusions, 50 (24.4%) developed sepsis, 35 (17.0%) presented with PDA, 6 (2.9%) developed IVH and 2 (1.0%) developed NEC. Other characteristics and associated systemic findings are listed in Table 2.

Totally 69 infants out of 207 (33.3%, 95%CI: 25.9%-42.2%) were recognized to have ROP. Mean BW and GA in ROP infants were significantly less than no ROP cases [1274±489 (530-3200) g *vs* 1916±550 (750-3700) g, *P*<0.001 and 29±2 (24-35)wk *vs* 33±3 (26-41)wk, *P*<0.001, respectively; Table 1]. Those infants with ROP were recognized as follows: stage 1 in 52.2% (36/69), stage 2 in 14.5% (10/69) and stage 3 in 33.3% (23/69). None of the infants developed stage 4 or 5. Zone I was detected among the infants with ROP in 4.3% (3/69), zone II in 58% (40/69), and zone III in 37.7% (26/69).

Of all ROP cases, 23 (33.3%, 95%CI: 21.1%-50%) received treatment due to severe ROP. Totally 16 cases were treated with laser in both eyes (22.2% of all ROP cases), and 7 infants received a combination of laser and intravitreal bevacizumab (0.625 mg) in the same session in both eyes (10.1% of all ROP cases). All cases received only one session of treatment.

We categorized the ROP cases into four groups based on BW and GA separately (Figure 1). It was demonstrated that both

Table 1 Baseline characteristics of the study population mean±SD; median (range)

Parameters	Total	No ROP	ROP		
			Total	Mild	Severe
Gestational age (wk)	32±3; 32 (24 to 41)	33±3; 33 (26 to 41)	29±2; 28 (24 to 35)	30±2; 29 (26 to 35)	28±2; 28 (24 to 32)
Mother age (y)	31±5; 31 (18 to 48)	31±5; 31 (20 to 48)	31±6; 31 (18 to 41)	30±5; 30 (18 to 41)	32±6; 33 (18 to 40)
Birth weight (g)	1701±610; 1650 (530 to 3700)	1916±550; 1860 (750 to 3700)	1274±489; 1200 (530 to 3200)	1393±542; 1245 (530 to 3200)	1036±221; 1050 (700 to 1480)
Bilirubin (mg/dL)	10±2.9; 10 (2 to 22.2)	10.2±3; 10 (2 to 22.2)	9.7±2.4; 9.7 (4 to 15)	9.9±2.6; 9.6 (4 to 15)	9.3±2.2; 10 (4 to 12)
NICU admission (d)	24±21; 18 (0 to 96)	16±14; 12 (0 to 90)	38±24; 31 (4 to 96)	32±22; 28 (5 to 95)	49±25; 47 (4 to 96)
Apgar score	7±2; 7 (0 to 10)	7±2; 7 (0 to 10)	6±2; 6 (1 to 9)	6±2; 7 (3 to 9)	4±2; 4 (1 to 8)
Mean platelet volume (fL)	10.4±1.2; 10.3 (8.1 to 13.2)	10.3±1.2; 10.2 (8.1 to 13.2)	10.5±1.1; 10.3 (8.5 to 12.5)	10.7±1.1; 10.7 (9.2 to 12.3)	10.5±1.1; 10.3 (8.5 to 12.5)
Platelet count ($\times 10^3/\mu L$)	254±114; 228 (22 to 646)	256±103; 238 (22 to 646)	250±133; 200 (40 to 581)	258±154; 200 (40 to 581)	241±104; 204 (54 to 450)
IGF-1 (nmol/L)	108.6±408.3; 31 (15 to 2518)	132.7±477.6; 32 (15 to 2518)	43.6±40.4; 30.5 (15 to 152)	38±24.3; 31 (18 to 65)	46±47.2; 30 (15 to 152)
Hemoglobin (mg/dL)	13±3; 13.3 (7.1 to 20.2)	13.7±2.8; 14 (7.1 to 20.2)	11.7±2.8; 11.1 (7.8 to 18)	12.6±2.7; 12.7 (8.1 to 18)	10.5±2.5; 9.7 (7.8 to 15.6)

ROP: Retinopathy of prematurity; NICU: Neonatal intensive care unit; IGF-1: Insulin-like growth factor-1.

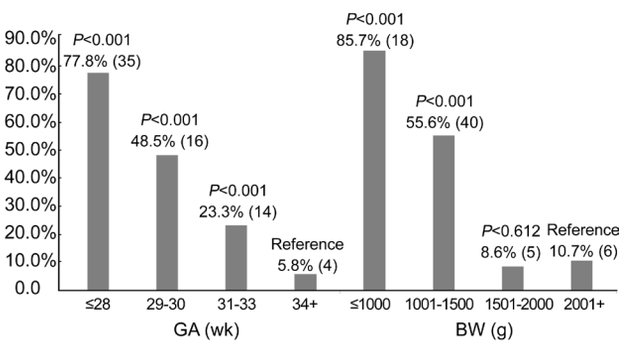

Figure 1 The rate of retinopathy of prematurity based on gestational age and birth weight The columns show the percentage (number) of retinopathy of prematurity cases in each GA and BW categories. *P* values are in comparison to the reference value. GA: Gestational age; BW: Birth weight.

lower BW and lower GA were significantly associated with increased incidence of ROP (*P* for trend <0.001). The highest ROP incidence was found in infants with BW≤1000 g (*P* for all comparisons <0.05) and in cases with GA≤28wk (*P* for all comparisons <0.05). None of the cases with severe ROP was found among infants with BW>1500 g or GA>32wk. Other clinical risk factors with corresponding incidences of ROP are presented in Tables 1 and 2.

Univariate and Multivariate Analysis Univariate analysis showed a significant relation between the incidence of ROP and GA, BW, NICU admission period, Apgar score, blood transfusion, surfactant usage, ARDS, sepsis, IVH and PDA. Severe ROP however, was significantly associated with GA, BW, NICU admission period, Apgar score, surfactant usage, ARDS, NEC, PDA as well as pre-eclampsia, eclampsia and HELLP syndrome (Table 3). The risk factors found to be significant in univariate analysis were used for multivariate logistic regression analysis. We utilized the likelihood ratio backward elimination method to obtain the most parsimonious model. It showed that only three independent risk factors including GA [relative risk (RR): 0.788], blood transfusion

Table 2 The incidence of ROP and severe ROP based on potential risk factors *n* (%)

Parameters	Total	No ROP	ROP		
			Total	Mild	Severe
Mother age (y)					
18-25	29 (14.4)	18 (62.1)	11 (37.9)	8 (27.6)	3 (10.3)
26-30	63 (31.3)	43 (68.3)	20 (31.7)	16 (25.4)	4 (6.3)
31-35	69 (34.3)	43 (62.3)	26 (37.7)	15 (21.7)	11 (15.9)
36+	40 (19.9)	29 (72.5)	11 (27.5)	6 (15.0)	5 (12.5)
Gender					
Female	100 (48.3)	66 (66.0)	34 (34.0)	23 (23.0)	11 (11.0)
Male	107 (51.7)	72 (67.3)	35 (32.7)	23 (21.5)	12 (11.2)
Blood transfusion					
No	115 (56.1)	99 (86.1)	16 (13.9)	15 (13.0)	1 (0.9)
Yes	90 (43.9)	39 (43.3)	51 (56.7)	29 (32.2)	22 (24.4)
Surfactant					
No	112 (55.2)	95 (84.8)	17 (15.2)	17 (15.2)	0
Yes	91 (44.8)	42 (46.2)	49 (53.8)	26 (28.6)	23 (25.3)
IVH					
No	199 (97.1)	136 (68.3)	63 (31.7)	42 (21.1)	21 (10.6)
Yes	6 (2.9)	2 (33.3)	4 (66.7)	2 (33.3)	2 (33.3)
GDM					
No	192 (93.7)	128 (66.7)	64 (33.3)	43 (22.4)	21 (10.9)
Yes	13 (6.3)	10 (76.9)	3 (23.1)	1 (7.7)	2 (15.4)
NEC					
No	203 (99.0)	137 (67.5)	66 (32.5)	43 (21.2)	23 (11.3)
Yes	2 (1.0)	1 (50.0)	1 (50.0)	1 (50.0)	0
ARDS					
No	59 (28.9)	54 (91.5)	5 (8.5)	5 (8.5)	0
Yes	145 (71.1)	84 (57.9)	61 (42.1)	38 (26.2)	23 (15.9)
Sepsis					
No	155 (75.6)	114 (73.5)	41 (26.5)	31 (20.0)	10 (6.5)
Yes	50 (24.4)	24 (48.0)	26 (52.0)	13 (26.0)	13 (26.0)
Pre-eclampsia, eclampsia or HELLP syndrome					
No	165 (80.5)	115 (69.7)	50 (30.3)	36 (21.8)	14 (8.5)
Yes	40 (19.5)	23 (57.5)	17 (42.5)	8 (20.0)	9 (22.5)
PDA					
No	171 (83.0)	124 (72.5)	47 (27.5)	37 (21.6)	10 (5.8)
Yes	35 (17.0)	14 (40.0)	21 (60.0)	8 (22.9)	13 (37.1)
Cesarean section					
No	30 (15.5)	18 (60.0)	12 (40.0)	8 (26.7)	4 (13.3)
Yes	164 (84.5)	111 (67.7)	53 (32.3)	35 (21.3)	18 (11.0)
Multiple gestation					
No	139 (67.1)	95 (68.3)	44 (31.7)	28 (20.1)	16 (11.5)
Yes	68 (32.9)	43 (63.2)	25 (36.8)	18 (26.5)	7 (10.3)

ROP: Retinopathy of prematurity; IVF: *In vitro* fertilization; IVH: Intraventricular hemorrhage; GDM: Gestational diabetes mellitus; NEC: Necrotizing enterocolitis; ARDS: Acute respiratory distress syndrome; PDA: Patent ductus arteriosus.

Table 3 Univariate analysis of risk factors for overall and severe retinopathy of prematurity

Risk Factors	Overall ROP incidence		Severe ROP incidence	
	RR (95%CI)	*P*	RR (95%CI)	*P*
Gestational age	0.747 (0.684 to 0.816)	<0.001	0.804 (0.655 to 0.987)	0.038
Mother age	0.984 (0.942 to 1.028)	0.470	1.040 (0.964 to 1.121)	0.314
Birth weight	0.857 (0.826 to 0.889)	<0.001	0.844 (0.767 to 0.929)	<0.001
Bilirubin (Maximum)	0.948 (0.846 to 1.062)	0.356	0.867 (0.691 to 1.087)	0.215
NICU admission (d)	1.023 (1.014 to 1.031)	<0.001	1.017 (1.002 to 1.032)	0.024
Apgar score	0.791 (0.700 to 0.893)	<0.001	0.742 (0.600 to 0.919)	0.006
Platelet volume	1.139 (0.797 to 1.629)	0.475	0.927 (0.569 to 1.509)	0.760
Platelet count	1.000 (0.997 to 1.002)	0.816	0.999 (0.996 to 1.003)	0.737
IGF-1	0.999 (0.992 to 1.005)	0.714	1.002 (0.984 to 1.020)	0.869
Blood transfusion	4.073 (2.323 to 7.142)	<0.001	6.902 (0.930 to 1.204)	0.059
Surfactant	3.548 (2.043 to 6.159)	<0.001	N/A	<0.001
ARDS	4.964 (1.995 to 2.354)	<0.001	N/A	<0.001
Sepsis	1.966 (1.203 to 3.213)	0.007	2.050 (0.899 to 4.675)	0.088
Gender	0.962 (0.689 to 1.343)	0.820	1.060 (0.594 to 1.890)	0.844
IVH	2.106 (1.031 to 4.303)	0.041	1.500 (0.538 to 4.183)	0.438
GDM	0.692 (0.305 to 1.570)	0.379	2.032 (0.729 to 5.666)	0.175
Pre-eclampsia, eclampsia or HELLP syndrome	1.402 (0.950 to 2.070)	0.088	1.891 (1.046 to 3.418)	0.035
PDA	2.183 (1.517 to 3.141)	<0.001	2.910 (1.624 to 5.212)	<0.001
Cesarean section	0.808 (0.519 to 1.258)	0.345	1.019 (0.474 to 2.192)	0.962
Multiple gestation	1.161 (0.821 to 1.643)	0.398	0.770 (0.411 to 1.443)	0.415

ROP: Retinopathy of prematurity; RR: Relative risk; CI: Confidence interval; IGF-1: Insulin-like growth factor-1; ARDS: Acute respiratory distress syndrome; IVH: Intraventricular hemorrhage; GDM: Gestational diabetes mellitus; PDA: Patent ductus arteriosus; N/A: Not available due to no observation in one of the levels.

(RR: 1.888) and BW (RR: 0.857) had significant correlation with overall ROP incidence, while none of the risk factors were found to have independent significant correlation with severe ROP (Table 4).

The sensitivity for diagnosis of ROP and severe ROP in this study was 95.7% and 100%, respectively, using the Iranian ROP screening criteria (BW≤2000 g or GA<34wk)[20], and 87% and 100% considering the AAP screening guidelines (Table 5).

Table 4 Independent risk factors for retinopathy of prematurity determined by multiple regression analysis

Risk factors	Overall ROP incidence	
	RR (95%CI)	*P*
Gestational age (1wk)	0.788 (0.711 to 0.873)	<0.001
Blood transfusion	1.888 (0.995 to 3.583)	0.052
Birth weight (100 g)	0.857 (0.813 to 0.903)	<0.001

ROP: Retinopathy of prematurity, RR: Relative risk, CI: Confidence interval.

DISCUSSION

ROP is one of the most common causes of preventable childhood blindness in both developing and developed countries[14]. Iran is undergoing the third epidemic of ROP, hence more studies on the incidence of ROP and its related risk factors is essential.

In our study, the incidence of ROP and severe ROP was 33.3% (69/207) and 11.1% (23/207), respectively. This was in line with other studies conducted in Iran, where the incidence of ROP was 34.5% in Tehran[15], 42.1% in Shiraz[23], 37.2% in the south of Iran[16], and 26.2% in the northeast of Iran[17]. Correspondingly, the incidence of severe ROP was 12.1% in Tehran[15], 9.5% in Shiraz[23], 7.5% in the north of Iran[24], and 8% in the southwest of Iran[25]. The small differences among the incidences of ROP in various regions of the country may be related to different genetics, NICU care, and methods of research. Compared to some other countries, the incidence of ROP in our study was higher than those of the United States (15.58%)[26], Bahrain (20.4%)[27] and China (12.7%)[12], and lower than those of Saudi Arabia (56%)[28] and Canada (40.4%)[29], while the incidence of severe ROP was higher than United States, China (2.3%)[12] and Bahrain (3.8%)[27], and nearly the same as Saudi Arabia (9%)[28] and Canada (9.2%)[29]. In our study, 85.7% of the infants with BW≤1000 g had ROP. This was higher than the reported rates from Tehran[15] (60.7%) and north of Iran (47.1%)[30] as well as the rates found in China (64%)[31] and Turkey (75.5%)[32]. However, it is similar to the Japanese reports (86.1%)[33].

Table 5 Sensitivity and specificity of Iran and United States screening criteria to detect retinopathy of prematurity in the present study %

Parameters	Iran ROP screening criteria		United States ROP screening criteria	
	Overall ROP incidence	Severe ROP incidence	Overall ROP incidence	Severe ROP incidence
Sensitivity	95.7	100	87	100
Specificity	18.8	15.8	72.5	59.2
Positive predictive value	37.1	12.9	61.2	23.5
Negative predictive value	89.7	100	91.7	100

ROP: Retinopathy of prematurity.

In the present study, univariate analysis showed a significant relationship between overall and severe ROP incidence and lower BW and GA. Both BW and GA have been identified as the main risk factors for the incidence of ROP by almost all previous studies[27,34-35]. We noted that NICU admission period, ARDS, surfactant usage and Apgar score were significant risk factors for overall and severe ROP incidence. Low Apgar score may be indicative of respiratory compromise immediately after birth and NICU admission period represents the duration of respiratory distress and hypoxemia which induce retinal hypoxia and promote ROP development[36-37]. We found significant relationships between ROP incidence and blood transfusion, sepsis, IVH and PDA. These findings are in agreement with previous studies which have shown an association between ROP and complex medical conditions[38-39]. In multivariate analysis, only three factors, *i.e.* BW, GA and blood transfusion, were shown as significant independent risk factors for ROP. Low BW and GA have been recognized as independent risk factors for the development of ROP in many studies[15,23,28,30]. Allegaert *et al*[40], Parekh *et al*[41] and Stutchfield *et al*[13], identified blood transfusion as a risk factor for ROP in multivariate regression analysis. Our results showed that blood transfusion is correlated with an 88% increase in the risk of ROP (RR: 1.888; Table 5). We did not find significant independent risk factors for severe ROP development in multivariate regression analysis, it might be due to few severe ROP cases (n=23) in our study.

For the first time in Iran, other risk factors such as MPV, platelet count, IGF-1 and hemoglobin levels (anemia) were investigated in our study. Unlike studies from other countries[6,9,42-43], we could not find any significant relationship between these risk factors and ROP incidence, perhaps due to the small sample size in our study.

The mean and range of GA [28±2 (24-32)wk] and BW [1036±221 (700-1480) g] of infants with severe ROP in our study was similar to the moderately developed countries such as Argentina [GA: 29 (27-31)wk and BW: 1156 (950-1360) g] and Thailand [GA: 29.2±2.5 (24-35)wk and BW: 1046±257 (710-1680 g)][44-45]. However a previous report by Karkhaneh *et al*[15] showed that the mean of GA (28.8±2.2wk) and BW (1257±348 g) of infants with severe ROP in Iran was more than those of developed countries. Considering these changes in the distribution patterns of GA and BW in ROP cases in Iran toward existing patterns in more developed countries, revision of the regional guidelines for ROP screening in Iran seems imperative. National Guideline for ROP screening in Iran (BW≤2000 g or GA<34wk) includes a wide range for GA and BW, cause over-referrals and an extra workload for ophthalmologists. Roohipoor *et al*[46] showed that by following the AAP guidelines (BW≤1500 g or GA≤30wk)[18], 8.4% of severe ROP infants would be missed. Therefore, they recommended the criteria of GA≤32wk and/or BW≤2000 g for the ROP screening program in Iran which would lead to a sensitivity of 100% for detection of severe ROP. In the present study, all of the infants affected by severe ROP were identified using the Iranian or AAP screening criteria. No case of severe ROP was found among infants with BW>1500 g or GA>32wk in our study; therefore, we recommend changing the ROP screening criteria to GA≤32wk or BW≤1750 g at least in Tehran (the capital city of Iran) which has sufficient trained ophthalmologists and good facilities in the field of ROP diagnosis and treatment. This new screening criteria would maintain 100% sensitivity for severe ROP while at the same time reduces the frequency of unnecessary examinations. We need more multicenter studies to recommend a narrower ROP screening criteria in the other cities of Iran.

Our study was powered by its prospective method and consideration of many risk factors among ROP cases; however, the relatively small sample size could be considered as a shortcoming in our study. It should be noted that the present study was conducted in a referral hospital, so our results cannot be generalized for the entire premature population.

In conclusion, the present study showed that the three factors of BW, GA and blood transfusion had independent significant relationships with the incidence of ROP in Iran, while having no effect on the severity of ROP. Therefore, in addition to the first two factors, blood transfusion should be considered as an ROP risk factor in premature infants. Considering the wide range of screening criteria in Iran as well as the results of this and other studies, a revision of these criteria is required in order to reduce costs and unnecessary examinations. We recommend changing the ROP screening criteria to GA≤32wk or BW≤1750 g in Tehran (the capital city of Iran).

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