

# Retinopathy of Prematurity: are we screening enough babies in Jordan?

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## ABSTRACT

**Objectives:** To assess the efficacy of the screening program for retinopathy of prematurity in Jordan and to determine the appropriate upper limits for screening in terms of gestational age and birth weight in premature babies in Jordan.

**Methods:** A prospective study conducted at the ophthalmology and neonatal department of Queen Rania Al Abdullah children's hospital between January and July 2017. All premature babies scheduled for retinopathy of prematurity screening exam which is performed at four to six weeks of age or at 31 week estimated gestational age were included in the study. Infants who died or were discharged against medical advice prior to the ROP screening were excluded from the study. Data were initially collected regarding the patient's gender, gestational age, birth weight, duration of admission to neonatal unit and oxygen therapy. The stage of ROP was determined through binocular ophthalmoscope and the RetCam. The type of treatment offered was reported. Results was analyzed and then compared to those in previous studies.

**Results:** One hundred and thirty- six (17%) out of 800 premature infants had ROP. The birth weight ranged between 0.8 and 2.4 kg (mean  $1.4\pm 0.6$ ) and the Gestational age (GA) ranged from 27 to 34 weeks (mean  $31\pm 1.5$ ). The rate of retinopathy of prematurity in infants with gestational age between 27 and 29 was (45.5%) compared to 21.0% and 7.1% in preterm infants of (28-30) weeks and infants above 30 weeks respectively. The rate of retinopathy was 37.1%, 18.4% and 13% in patients with birth weight less than 1 kg, (1-1.5) kg and above 1.5 kg respectively. Stage I, II, III, and IV were found in 36.0%, 18.4%, 44.1%, and 1.5% respectively. No patient in this study was reported to have stage V disease. Sixty-two patients (10.3%) required treatment.

**Conclusion:** The rate of Retinopathy of Prematurity among Jordanian premature infants at Queen Rania Al Abdullah children hospital was 17%. The rate and severity of Retinopathy of prematurity were higher in patients with low birth weight and low gestational age. Some premature infants of birth weight of more than 1.5 kg developed retinopathy requiring treatment. It is recommended to extend the upper limit of retinopathy of prematurity screening program in Jordan to include preterm infants with a birth weight up to 2 Kgs. Where the screening program was more effective in detecting retinopathy and the more appropriate management was able to be presented to the patients.

**Keywords:** Birth Weight, Gestational Age, Retinopathy of Prematurity.

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## Introduction

Retinopathy of Prematurity (ROP), formerly named retrolental fibroplasias, is a blinding

disease of preterm infants. During the intra uterine life and at gestational age of 16 weeks, the angioblasts migrate toward the periphery of the retina to form the retinal

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vasculature reaching the ora serrata at the nasal side at 36 weeks and the temporal at 40 weeks of gestation. Excessive hyperoxia leads to cessation of the retinal vascularization, the vascularity of that retina will not meet the metabolic activity and lead to hypoxia. To compensate for this demand growth factor driven vasoproliferation will be stimulated, which may ultimately cause fibrosis and retinal detachment.<sup>(1,2)</sup> A high concentration of oxygen supplement in incubators for the premature is the leading cause for such condition. Lowering the oxygen concentration may reduce the risk of ROP but may be associated with higher mortality and morbidity.<sup>(3)</sup> In some countries 100% oxygen is still used without monitoring.<sup>(4)</sup> Although a lot of studies have been conducted worldwide, the minimum effective oxygen saturation which can improve the survival without impact on the retina is still unknown.<sup>(5)</sup> The 1984 international classification for ROP was updated in 2005 and 2013.<sup>(6)</sup> Such a classification system is important to evaluate the severity of the disease and the treatment options. Infants scheduled for screening are those with birth weights  $\leq 1500$  g or a GA of 30 weeks or less, as well as selected infants with birth weights between 1500 g and 2000 g or a gestational age (GA)  $>30$  weeks who were believed to be at high risk for ROP. The first recommended screening exam which is adopted by our institute is performed at four to six weeks of age or at 31 week estimated GA.<sup>(7)</sup> The aim of this study was to assess the efficacy of the screening program for ROP and to determine the appropriate upper limits for ROP screening in terms of gestational age and birth weight in premature babies in Jordan.

## Methods

This is a prospective study conducted at the ophthalmology department of Queen Rania Al- Abdullah children's hospital between

January and July 2017. All premature babies scheduled to have ROP screening exam were included in the study. Infants who died or discharged against medical advice prior to the ROP screening and those who underwent inadequate follow up were excluded from the study. Data were initially collected regarding patient's gender, gestational age, birth weight, duration of admission to neonatal unit and oxygen therapy. The stage of ROP was determined through indirect binocular ophthalmoscope and the RetCam. The type of treatment offered was reported for infants with ROP. Data were collected and analyzed using the excel and compared to the results revealed by other studies conducted in Jordan, regional countries and worldwide.

## Results

Eight hundreds preterm infants were subjected to ROP screening, 136 of them (17%) were found to have ROP; 51.5% of them were males (ratio 1.06:1). The birth weight ranged between 0.8 and 2.4 kg (mean  $1.4 \pm 0.6$ ) and the GA ranged between 27 and 34 weeks (mean  $31 \pm 1.5$ ). Table I summarizes the distribution of the patients regarding GA in relation to oxygen concentration used.

Stage 1 ROP was found in 49 patients (36.0%) while stage 2, 3 and 4 were found in 18.4%, 44.1% and 1.5% of patients respectively. Plus disease was found in 7 patients (5.1%). No patient was reported to have stage V ROP. Laser treatment was needed in 62 patients (45.6%) while intra vitreal Bevacizumab (Avastin) was given in 9 patients (6.6%). Twelve patients were twins and 3 patients were triplets. For patients with stages 1 and 2 only observations were offered, while laser treatment, intra vitreal Bevacizumab and surgery were the treatment options for stage 3 or more. Figure 1 and 2 summarizes the severity of the ROP among the patients in relation to GA and birth weight respectively.

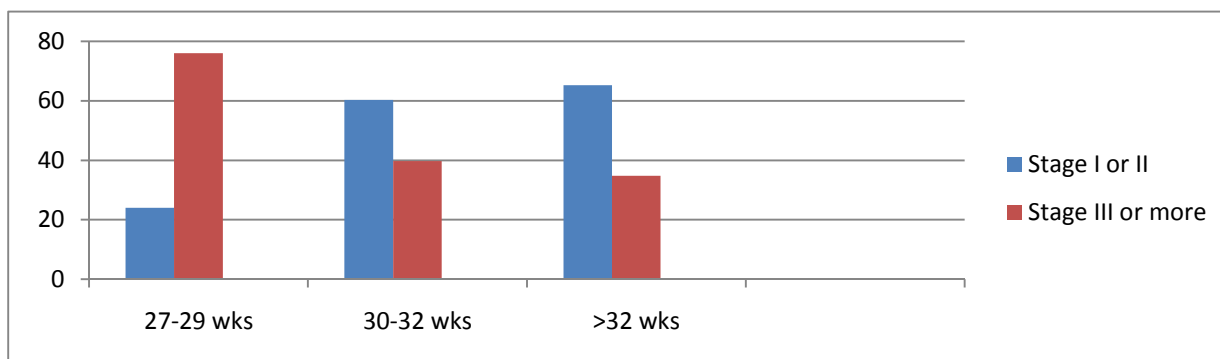
**Table I:** ROP in relation to GA in relation to Oxygen concentration.

Gestational age	27-29wks	30-32wks	>32wks	Total
No. of patients with ROP (%)	25 (18.4%)	88 (64.7%)	23 (16.9%)	136(100%)
Total No. of patients	55 (6.9%)	420 (52.5%)	325 (40.6%)	800(100%)
Frequency of ROP	25/55 (45.5%)	88/420 (21.0%)	23/325 (7.1%)	136/800 (17%)
Oxygen concentration	60%	60%	40%	
Duration of admission	4 weeks	3 weeks	2 weeks	

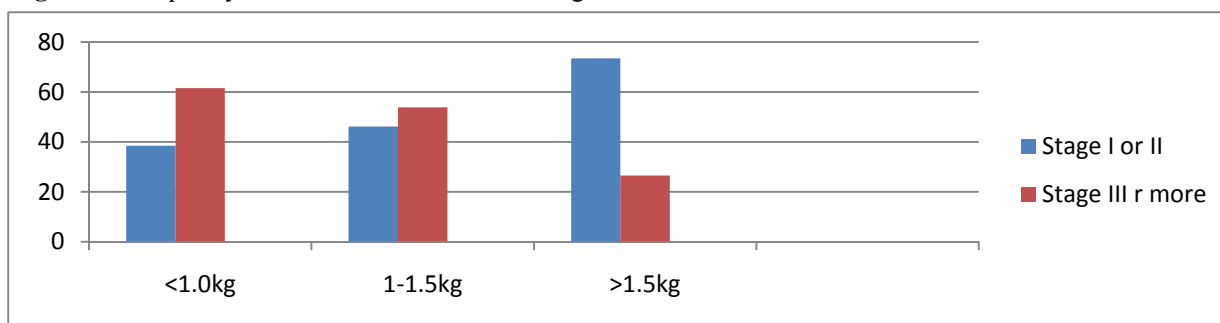
**Table II:** ROP in relation to patient's weight.

Weight	<1.0 kg	1-1.5 kg	>1.5 kg	Total
No. of patients with ROP (%)	13 (9.6%)	80 (58.8%)	43 (31.6%)	136 (100%)
Total No. of patients	35 (4.4%)	434 (54.3%)	331 (41.3%)	800 (100%)
Frequency of ROP	13/35 (37.1%)	80/434 (18.4%)	43/331 (13.0%)	136/800 (17%)

**Fig 1:** The frequency of ROP in relation to GA.



**Fig 2:** The frequency of ROP in relation to birth weight



## Discussion

ROP is a preventable cause of blindness among children in the world.<sup>(8)</sup> The incidence varies from country to country; the rate of ROP is between 5 and 8 % in developed countries compared to 30 % in the world.<sup>(9)</sup> In our study we found that 136 premature (17%) out of 800 had ROP. This incidence was lower than that found in regional countries like Iran (30%) and Saudi Arabia (56%) and it was much lower than that found in previous studies conducted in Jordan by Gharaibeh *et al* and Al-Bdour *et al* who found the rate of ROP to be 28.6% in 2007 and 44% in 2004 respectively.<sup>(10,11)</sup> This difference may be attributed to the lower average birth weight and GA in their studies compared with ours.<sup>(12,13)</sup> Low birth weight and GA are known to be associated with higher incidence of ROP.<sup>(14)</sup> In addition, this

decline in the ROP rate may reflect the improvement in the antenatal care and the efficacy of the ROP screening programs. The rate of ROP was much higher in infants with GA between 27 and 29 (45.5%) compared to 21.0% and 7.1% in preterm infants of 28-30 weeks and infants above 30 weeks respectively (*P* value <0.05). Careful and early screening of infants with low GA is highly recommended to prevent visual loss as a result of ROP. Although the same oxygen concentration was used in patients with GA of (27-29) weeks and (30-32) weeks the frequency of ROP was higher in the former group due to lower GA. The lower oxygen concentration used in patients above 32 weeks was associated with much lower incidence of ROP. However, higher GA and birth weights found in this group may also contribute to the lower incidence of ROP.<sup>(15)</sup> An oxygen concentration of 60% and 40%

are considered to be low when compared to that used in other parts of the world.<sup>(5,16)</sup> Using this concentration reduces the risk of ROP. Therefore, a comprehensive study is recommended for our institute to find out whether this concentration is not associated with higher mortality rate. Retinopathy of prematurity was statistically significantly ( $P$  value  $<0.05$ ) more frequent in patients with a birth weight of less than 1 kg. Therefore, effective screening for extremely low birth weight preterm is mandatory for early detection and treatment of ROP.<sup>(8)</sup> The current US guidelines updated in 2013, recommend screening for infants with birth weight of 1.5 kg or less. In our study 43 patients of 331 (17%) with birth weight more than 1.5 kg had ROP and 26.6% of those had severe ROP that required treatment; the highest birth weight recorded in those patients was 1.95 kg. No preterm infants with birth weight above 2 Kgs was found to have ROP. So we highly recommend enrolling preterm infants with birth weight of 1.5-2.0Kgs in the screening program. Stage 1, 2, 3, and 4 were found in 36.0%, 18.4%, 44.1%, and 1.5% respectively. No patient was reported to have stage 5, this may reflect the effectiveness of the screening program and the improvement of antenatal and neonatal care of patients. It is estimated that 10% of infants screened for ROP develop severe forms of the disease and require treatment.<sup>(17)</sup> In our study, 62 ROP patients (10.3%) required treatment which was comparable to international studies. Not only low birth weight and early GA associated with higher rate of ROP, but they were also significantly associated with more severe forms of ROP ( $P$  value  $<0.05$ ); ROP (stage 3 or more) was found in 76% and 61.5% in patients of 27-28 week GA and less than 1kg birth weight respectively, compared with 34.8% and 26.6% in patients of  $>32$  week GA and  $>1.5$ kg birth weight respectively. There was no statistical significance association of rate of ROP with gender or multiple pregnancies. This study was conducted at the ophthalmology and neonatal department of Queen Rania Al Abdullah children's hospital by a pediatric ophthalmologists and neonatologist. In addition, the retina exam was performed by

using the RetCam and indirect biomicroscope; this all improved the yield and accuracy of the fundus exam. The frequency of ROP in our study was higher than that of developed countries but it was much lower than that of regional countries and previous Jordanian studies conducted in 2004 and 2011. The incidence and severity of ROP were significantly associated with low birth weight and low GA. Finally, this study showed that preterm infants of birth weight above 1.5 kg still have a chance to develop ROP which may need treatment, so we recommend continuing screening those patients when we adopt using the international guidelines for ROP screening particularly the US ones.

## Conclusion

The rate of Retinopathy of prematurity among Jordanian premature infants at Queen Rania Al Abdullah children's hospital was 17%. The rate and severity of Retinopathy of Prematurity were higher in patients with low birth weight and low gestational age. Some premature infants of birth weight of more than 1.5 kg developed retinopathy which required treatment. It is recommended to extend the upper limit of retinopathy of prematurity screening program in Jordan to include preterm infants with birth weight up to 2 Kgs.

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