Title	Screening for retinopathy of prematurity and treatment outcome in a tertiary hospital in Hong Kong
Author(s)	IU, LPL; Lai, CHY; Fan, MCY; Wong, YHI; Lai, JSM
Citation	Hong Kong Medical Journal, 2016, v. 23 n. 1, p. 41-47
Issued Date	2016
URL	http://hdl.handle.net/10722/248295
Rights	Hong Kong Medical Journal. Copyright © Hong Kong Academy of Medicine Press.; This work is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License.

Screening for retinopathy of prematurity and treatment outcome in a tertiary hospital in Hong Kong

Lawrence PL lu *, Connie HY Lai, Michelle CY Fan, Ian YH Wong, Jimmy SM Lai

A B S T R A C T

Introduction: Studies on the prevalence and severity of retinopathy of prematurity in the local population are scarce. This study aimed to evaluate the prevalence, screening, and treatment outcome of retinopathy of prematurity in a tertiary hospital in Hong Kong.

Methods: This cross-sectional study with internal comparison was conducted at Queen Mary Hospital, Hong Kong. The study evaluated 89 premature infants who were born at the hospital and were screened for retinopathy of prematurity, in accordance with the 2008 British Guidelines, between January 2013 and December 2013. The prevalences of retinopathy of prematurity and severe retinopathy requiring treatment were studied.

Results: The mean (± standard deviation) gestational age at birth was 30^{+2} weeks ± 16.5 days (range, 24^{+1} to 35^{+5} weeks). The mean birth weight was 1285 g ± 328 g (range, 580 g to 2030 g). A total of 15 (16.9%) infants developed retinopathy of prematurity and three (3.4%) required treatment. In a subgroup analysis of extremely-low-birth-weight infants of <1000 g, 70.6% developed retinopathy of prematurity and 17.6% required treatment. Multivariate logistic regression analysis suggested low birth weight and patent ductus arteriosus were significantly associated with development of retinopathy of prematurity (P<0.001 and P=0.035, respectively). Among the three infants who received treatment for severe retinopathy of prematurity, all regressed successfully after one laser treatment.

Conclusions: Retinopathy of prematurity is a significant problem among premature infants in Hong Kong, especially those with extremely low birth weight. Our screening service for retinopathy of prematurity was satisfactory and treatment results were good. Strict adherence to international screening guidelines and vigilance in infants at risk are key to successful management of retinopathy of prematurity.

Hong Kong Med J 2017;23:41–7
DOI: 10.12809/hkmj154811

LPL lu *, FRCSEd (Ophth), FHKAM (Ophthalmology)
CHY Lai, FHKAM (Ophthalmology)
MCY Fan, FRCSEd (Ophth), FHKAM (Ophthalmology)
IYH Wong, FRCOphth, FHKAM (Ophthalmology)
JSM Lai, FRCOphth, FHKAM (Ophthalmology)

Department of Ophthalmology, Queen Mary Hospital, The University of Hong Kong, Pokfulam, Hong Kong

* Corresponding author: lawipl@hku.hk

This article was published on 30 Dec 2016 at www.hkmj.org.

New knowledge added by this study

- Low birth weight and patent ductus arteriosus were significantly associated with the development of retinopathy of prematurity (ROP).

Implications for clinical practice or policy

- ROP is a significant problem among premature infants in Hong Kong, especially those with extremely low birth weight.
- Strict adherence to international screening guidelines and vigilance in high-risk infants are key to successful ROP management.

Introduction

Retinopathy of prematurity (ROP) is a retinal vascular disease that affects premature infants in whom the retinal vasculature is not fully developed at the time of birth. The hyperoxic environment after birth—inclusive of room air—compared with the relative hypoxic intra-uterine environment suppresses the growth of retinal vessels (phase 1). Subsequently, growth of the retina increases metabolic demand and, in the background of incomplete retinal vascularisation, results in retinal hypoxia and ROP development (phase 2).[1-3] Retinopathy of prematurity is characterised by the presence of abnormal retinal fibrovascular proliferation. Severe disease will progress to total retinal detachment and blindness if there is no intervention during the critical treatment

香港一所提供第三層醫療服務的醫院中早產兒視網膜病變篩查的成效和治療結果

姚沛良、黎匡怡、范靖琰、王逸軒、黎少明

引言：本地有關早產兒視網膜病變的發生率以及其嚴重程度的研究很少。本研究旨在評估香港一所提供第三層醫療服務的醫院中早產兒視網膜病變的患病率、篩查成效和治療結果。

方法：這內部比較的橫斷面研究在香港瑪麗醫院內進行。根據2008年英國皇家兒科學和兒童保健學院的指引，本研究評估2013年1月至12月期間在上述醫院出生的89名早產兒，並為他們進行視網膜病變篩查。探討他們視網膜病變的患病率，以及需要治療的嚴重視網膜病變病例。

結果：早產兒出生時的平均胎齡為30^{+2}週（標準差16.5天；介乎24^{+1}至35^{+5}週）。平均出生體重為1285 g（標準差328 g；介乎580 g至2030 g）。共有15名（16.9%）嬰兒出現早產兒視網膜病變，當中3例（3.4%）需要治療。在極低出生體重嬰兒（<1000 g）的亞組分析中發現70.6%有早產兒視網膜病變，當中17.6%需要治療。多變量邏輯迴歸分析顯示低出生體重和開放性動脈導管與早產兒視網膜病變的發展有關（P值分別為<0.001和0.035）。接受治療嚴重視網膜病變的3例早產兒在接受一次激光治療後均成功治癒。

結論：視網膜病變是香港早產兒的一個重要問題，特別是出生體重極低的兒童。我們的早產兒視網膜病變篩查服務令人滿意，治療結果良好。嚴格遵守國際篩選指南和對處於危險狀態的嬰兒提高警覺是成功治療早產兒視網膜病變的關鍵。

period. Such retinopathy is one of the leading causes of visual impairment in children.[4-6]

The risk factors for ROP include low gestational age (GA), low birth weight (BW), presence of co-morbidities (eg patent ductus arteriosus [PDA], necrotising enterocolitis (NEC), intraventricular haemorrhage [IVH]), and a high level of supplemental oxygen.[7-9] Those born at extreme prematurity and with extremely low birth weight (ELBW) are at high risk of severe ROP development. The British Guidelines published by the Royal College of Paediatrics and Child Health in 2008 recommended screening for ROP in premature infants with GA of <32 weeks or BW of <1501 g.[10] The American Guidelines published by the American Academy of Pediatrics in 2013 recommended screening for ROP if GA was ≤30 weeks or BW ≤1500 g. Selected infants with BW of 1500 to 2000 g or GA of >30 weeks with an unstable clinical course should also be screened if they were assessed by the attending neonatologist to be at high risk of ROP.[11] Since neonatal intensive care units and standards of health care have improved significantly in the past decade, more extreme preterm infants are surviving and a higher risk of ROP development is to be expected.[12,13]

The revised International Classification of Retinopathy of Prematurity was published in 2005.[14] In this revised version, ROP was classified into five stages depending on the severity of retinal fibrovascular proliferation and into three zones depending on the location of vascularisation.[14] Plus disease is characterised by the presence of severe retinal venous dilatation and arteriolar tortuosity, iris vascular engorgement, poor pupillary dilatation, and vitreous haze.[14] Presence of plus disease indicates high disease activity.[14] Aggressive posterior ROP is an uncommon, severe form of ROP characterised by posterior vascularisation, prominent plus disease, and rapid progression.[14] Timely treatment is required for severe ROP to prevent retinal detachment and vision loss. Current guidelines suggest treatment if the ROP is type 1 pre-threshold defined by the Early Treatment for Retinopathy of Prematurity (ETROP) study,[15] that is: (i) zone I, any stage of ROP, with plus disease; (ii) zone I, stage 3 ROP, with or without plus disease; or (iii) zone II, stage 2 or 3 ROP, with plus disease.[10,11]

The traditional mainstay of treatment is laser photocoagulation to ablate all avascular areas and reduce the ischaemic stress to allow the retinal fibrovascular proliferation to regress.[10,11] Intravitreal injection of anti–vascular endothelial growth factor (anti-VEGF) agent has recently been advocated if ROP is in zone I, stage 3 with plus disease or aggressive posterior ROP.[16] Operation with vitrectomy or scleral buckle surgery is required if retinal detachment has occurred but the results are often unsatisfactory.[17,18] Proper screening and timely treatment are thus important measures to prevent retinal detachment and vision loss.

The prevalence of ROP and severe ROP that requires treatment vary among different countries. The reported prevalence of ROP ranged from 12.6% to 44.5%[13,19-23] and that of severe ROP requiring treatment ranged from 1.5% to 11.7% in other countries.[13,19-23] In Hong Kong, studies that report the prevalence and severity of ROP are scarce.[24,25] The aim of this study was to evaluate the ROP prevalence, screening, and treatment outcome in a tertiary hospital in Hong Kong.

Methods

This was a retrospective cross-sectional study with internal comparison in which the medical records of eligible subjects were reviewed. All premature infants who were born at Queen Mary Hospital and had ROP screening performed between 1 January 2013 and 31 December 2013 were included. In this hospital, all infants are screened if the British screening criteria are met—GA of <32 weeks or BW of <1501 g. Those who died before ROP screening could be performed were excluded from this study. This study was done in accordance with the principles outlined in the Declaration of Helsinki.

All ROP screening was performed by two ophthalmologists who had experience in screening and treating ROP. All examinations were performed

with binocular indirect ophthalmoscopy following pupil dilatation by topical mydriatic medication. The severity of ROP was graded according to the revised International Classification of Retinopathy of Prematurity.[14] The screening protocol followed the British Guidelines published in 2008[10]:

- First ROP screening was performed at 30 to 31 weeks postmenstrual age (PMA) for infants born before 27 weeks GA, and at 4 to 5 weeks postnatal age for infants born at or after 27 weeks GA.
- Regular ROP screening was performed every 1 to 2 weeks, and more frequent examinations at 1 week or less if the following features were present: (i) vascularisation ending in zone I or posterior zone II; (ii) presence of plus or pre-plus disease; or (iii) presence of stage 3 ROP.
- Treatment was initiated within 48 to 72 hours if the ROP was type 1 pre-threshold defined by the ETROP study[15] with the following features: (i) zone I, any stage of ROP, with plus disease; (ii) zone I, stage 3 ROP, with or without plus disease; or (iii) zone II, stage 2 or 3 ROP, with plus disease.
- ROP screening was terminated in infants who did not develop ROP and in whom vascularisation had extended into zone III after 36 weeks PMA, or in those who developed ROP that did not meet treatment criteria and had subsequently regressed.

Data recorded included GA, BW, presence of co-morbidities, most severe ROP stage, any treatment given, and the treatment outcome. If the ROP stage was asymmetrical between the two eyes in an individual infant, the more severe ROP stage was measured.

Primary outcome measures included the prevalence of ROP of any stage and severe ROP that required treatment. Secondary outcome measures included association between risk factors of interest and risk of ROP development, and treatment outcome. The risk factors of interest studied included low GA, low BW, presence of respiratory distress syndrome (RDS), PDA, sepsis, NEC, IVH and the need for blood transfusion.

Statistical analysis

The Statistical Package for the Social Sciences (Windows version 23.0; SPSS Inc, Chicago [IL], US) was used to perform the statistical analysis. All continuous demographic data are expressed as mean ± standard deviation and categorical data are expressed as number (%). Further, GA and PMA are represented as number of weeks and the remaining days not completing a week written in superscript, eg 32 weeks and 5 days represented by 32^{+5} weeks. Chi squared test was used to evaluate the difference among subgroups for ROP development. Fisher's exact test was used when the expected frequency of a cell in a table was <5. Risk factors that might predict ROP development were evaluated in univariate logistic regression analyses to calculate the odds ratio (OR) and 95% confidence interval. If there was more than one factor associated with a P value of <0.05 in univariate level, the risk factors would be entered into a multivariate logistic regression analysis with backward stepwise method. P<0.05 was considered to be statistically significant. All tests were two-sided.

Results

Demographic data

A total of 92 infants met the British screening criteria during the study period of whom three died before ROP screening could be performed and were excluded from this study. Among the 89 infants screened, 52.8% were male. There were 49 (55.1%) singletons, 37 (41.6%) twins, and three (3.4%) triplets. The mean GA was 30^{+2} weeks ± 16.5 days (range, 24^{+1} weeks to 35^{+5} weeks; median, 30^{+4} weeks). The mean BW was 1285 g ± 328 g (range, 580 g to 2030 g; median, 1340 g). The distribution of infants in relation to GA and BW is shown in Table 1.

Prevalence of retinopathy of prematurity

Of the 89 infants screened, 15 (16.9%) developed ROP at a mean time of 34^{+1} weeks ± 13.0 days (range, 31^{+5} weeks to 38^{+4} weeks; median, 33^{+4} weeks), and three (3.4%) required treatment at a mean time of 40^{+2} weeks ± 9.6 days (range, 39^{+2} weeks to 41^{+6} weeks; median, 39^{+5} weeks). Nine (10.1%) infants developed stage 1 ROP, three (3.4%) developed stage 2 ROP, three (3.4%) developed stage 3 ROP, and none developed stage 4 or 5 ROP (Table 2).

Among the 15 infants who developed ROP, their mean GA was 27^{+1} weeks ± 14.4 days (range, 24^{+1} weeks to 30^{+2} weeks; median, 27^{+5} weeks) and mean BW was 846 g ± 276 g (range, 580 g to 1530 g; median, 790 g).

In subgroup analysis, among the 17 ELBW infants of <1000 g, 12 (70.6%) developed ROP and three (17.6%) required treatment. Among the 12 extremely preterm infants with GA of <28 weeks, eight (66.7%) developed ROP and three (25.0%) required treatment (Table 2).

When the 2013 American screening criteria were applied retrospectively, 78 (87.6%) infants met the criteria. In the 11 (12.4%) infants whose GA and BW exceeded the 2013 American screening criteria, none of them developed any ROP.

Risk factors for development of retinopathy of prematurity

In univariate logistic regression analysis, factors associated with risk of ROP development included

low GA (OR=1.129 for each day decrease; P<0.001), low BW (OR=1.007 for each g decrease; P<0.001), RDS (OR=4.952; P=0.044), PDA (OR=12.904; P<0.001), sepsis (OR=4.787; P=0.013), and need for blood transfusion (OR=11.786; P<0.001) [Table 3].

In multivariate logistic regression analysis, factors associated with risk of ROP development included low BW (OR=1.006 for each g decrease; P<0.001) and PDA (OR=5.749; P=0.035) [Table 3].

TABLE 1. Demographic data of 89 infants who were screened for retinopathy of prematurity

Demographics	No. (%) of infants (n=89)
Gender	
Male	47 (52.8)
Female	42 (47.2)
No. of gestations	
Singleton	49 (55.1)
Twins	37 (41.6)
Triplets	3 (3.4)
Gestational age (weeks)	
<26	5 (5.6)
26 to <28	7 (7.9)
28 to <30	19 (21.4)
30 to <32	41 (46.1)
≥32	17* (19.1)
Birth weight (g)	
<1000	17 (19.1)
1000 to <1500	54 (60.7)
≥1500	18† (20.2)

* 17 Infants with gestational age of ≥32 weeks were screened because their birth weight was <1501 g

† 18 Infants with birth weight of ≥1500 g were screened because their gestational age was <32 weeks

Treatment of retinopathy of prematurity

Three infants developed severe ROP that required treatment (Table 4). Their mean GA was 25^{+1} weeks ± 7.5 days (range, 24^{+1} weeks to 26^{+2} weeks; median, 25^{+1} weeks) and mean BW was 708 g ± 79 g (range, 660 g to 800 g; median, 665 g). All received indirect diode laser photocoagulation treatment and all regressed after one laser treatment. No supplementary laser, intravitreal injection of anti-VEGF agent, or surgery was necessary.

Discussion

This retrospective study identified the prevalence of ROP and severe ROP requiring treatment among premature infants in a tertiary hospital in Hong Kong. We observed a prevalence of ROP of 16.9% and that of severe ROP requiring treatment was 3.4%. Our prevalence was comparable to or less than that reported in most other countries. The reported prevalences of ROP were 29.2% in Singapore,[19] 37.8% in Southern Taiwan,[20] 21.6% in Southern India,[21] 12.6% in England,[13] 21.9% in Netherlands,[22] and 44.5% in Brazil.[23] The reported prevalences of severe ROP requiring treatment were 4.8% to 5.0% in Singapore,[19] 11.7% in Southern Taiwan,[20] 6.7% in Southern India,[21] 1.5% in England,[13] and 1.8% in Brazil.[23] In mainland China, the ROP screening included bigger infants with BW of up to 2000 g and GA of up to 34 weeks, and the reported prevalences of ROP and severe ROP requiring treatment were 17.8% and 6.8%, respectively.[26] Since the risk of ROP among large infants is known to be small, the prevalence of ROP in mainland China could not be

TABLE 2. Outcome of retinopathy of prematurity (ROP) screening among 89 infants in relation to birth weight and gestational age

Outcome	Birth weight (g)				Gestational age (weeks)			
	<1000 (n=17)	1000 to <1500 (n=54)	≥1500 (n=18)	P value*	<28 (n=12)	28 to <32 (n=60)	≥32 (n=17)	P value*
Any stage of ROP	12 (70.6%)	2 (3.7%)	1 (5.6%)	<0.001	8 (66.7%)	7 (11.7%)	0	<0.001
Stage of ROP								
Stage 1	6 (35.3%)	2 (3.7%)	1 (5.6%)	0.003	3 (25.0%)	6 (10.0%)	0	0.064
Stage 2	3 (17.6%)	0	0	0.006	2 (16.7%)	1 (1.7%)	0	0.067
Stage 3	3 (17.6%)	0	0	0.006	3 (25.0%)	0	0	0.002
Stage 4	0	0	0	1.000	0	0	0	1.000
Stage 5	0	0	0	1.000	0	0	0	1.000
Severe ROP requiring treatment	3 (17.6%)	0	0	0.006	3 (25.0%)	0	0	0.002
Aggressive posterior ROP	0	0	0	1.000	0	0	0	1.000
Retinal detachment	0	0	0	1.000	0	0	0	1.000

* Fisher's exact test

TABLE 3. Univariate and multivariate logistic regression analyses of risk factors in relation to development of retinopathy of prematurity of any severity among 89 infants screened

	Odds ratio	95% Confidence interval	P value
Univariate			
Low gestational age (days)	1.129	1.067-1.194	<0.001
Low birth weight (g)	1.007	1.004-1.010	<0.001
RDS	4.952	1.043-23.523	0.044
PDA	12.904	3.547-46.949	<0.001
Sepsis	4.787	1.388-16.515	0.013
NEC	3.000	0.770-11.682	0.113
IVH	1.135	0.224-5.738	0.878
Blood transfusion	11.786	3.265-42.548	<0.001
Multivariate			
Low gestational age (days)		(Excluded from multivariate logistic model)	
Low birth weight (g)	1.006	1.003-1.009	<0.001
RDS		(Excluded from multivariate logistic model)	
PDA	5.749	1.129-29.271	0.035
Sepsis		(Excluded from multivariate logistic model)	
Blood transfusion		(Excluded from multivariate logistic model)	

Abbreviations: IVH = intraventricular haemorrhage; NEC = necrotising enterocolitis; PDA = patent ductus arteriosus; RDS = respiratory distress syndrome

TABLE 4. Characteristics and outcome of infants who received treatment for retinopathy of prematurity

Patient No.	Gestational age (weeks)	Birth weight (g)	Severity of ROP and time of development	Types and time of treatment	Outcome
1	24^{+1}	660	BE zone 2, stage 3, with plus disease at PMA 41^{+4} weeks	BE laser at PMA 41^{+6} weeks	ROP regressed
2	26^{+2}	800	BE zone 2, stage 3, with plus disease at PMA 38^{+6} weeks	BE laser at PMA 39^{+2} weeks	ROP regressed
3	25^{+1}	665	BE zone 2, stage 3, with plus disease at PMA 39^{+5} weeks	BE laser at PMA 39^{+5} weeks	ROP regressed

Abbreviations: BE = both eyes; PMA = postmenstrual age; ROP = retinopathy of prematurity

directly compared with our study.

Severe ROP is more prevalent in ELBW infants. Our study showed the prevalence of ROP was 70.6% and that of severe ROP requiring treatment was 17.6% in ELBW infants of <1000 g. This was comparable to another local study in Hong Kong in which 53.4% of ELBW infants developed ROP and 14.5% developed severe ROP requiring treatment.[25] Our results are also comparable to those of other countries, where the prevalences of ROP and severe ROP requiring treatment in ELBW infants were 55.4% and 13.7% respectively in Singapore,[19] 70.7% and 29.3% respectively in Southern Taiwan,[20] 61.3% and 28.4% respectively in Northern Taiwan,[27] and 55.9% and 19.4% respectively in Turkey.[28] In this study, multivariate logistic regression analysis showed the risk of ROP development was significantly associated with low BW and presence of PDA. The association between PDA and risk of ROP development has been shown in previous studies.[8,9] It has been postulated that persistent left-to-right shunt results in low systemic blood flow and retinal ischaemia, and thus is associated with higher risk of ROP development.[8,29] In addition, use of indomethacin to close PDA might reduce retinal blood flow and contribute to ROP development.[8,30]

Dilated fundal examination in ROP screening is a stressful event for premature infants. It is important to screen only those who are at risk to avoid unnecessary examination and stress. In this study, 11 infants would not have been screened if the 2013 American screening criteria were used and none of them developed any ROP. This may suggest that the 2013 American Guidelines are more appropriate than the 2008 British Guidelines in reducing unnecessary examination.

In our study, all severe ROP (100%) regressed after one laser treatment without the need for repeat treatment. No infants developed stage 4 or above ROP. This reflects a good standard of neonatal care in

Hong Kong. In Southern Taiwan, 16.9% progressed to stage 4 or 5 ROP requiring further intervention after initial treatment.[20] In mainland China, 4.2% of stage 3 ROP and 28.6% of aggressive posterior ROP progressed to retinal detachment after initial treatment.[26]

Our study highlights the importance of proper screening and timely treatment to prevent retinal detachment and severe vision loss due to ROP. We recommend strict adherence to international screening guidelines, and all ROP screening should be performed by ophthalmologists with dilated fundal examination.[10] Since ELBW infants have a high risk of ROP and need for treatment, early parent education and good communication with anticipation for treatment will be helpful. For premature infants transferred from other hospitals for non-ophthalmological conditions, attention should be paid to the ROP screening record and examinations should be performed if the screening criteria are met. Good communication between hospital units is crucial to ensure continuous care and that these infants do not miss ROP screening and thus the window of opportunity for treatment.

There were several limitations in this study. First, the sample size was small. Second, due to the retrospective design, this study was not able to evaluate other potential risk factors that might increase the risk of ROP development. The level of oxygen therapy was not evaluated because it could not be assessed accurately in view of frequent changing of arterial oxygen saturation level and percentage of oxygen administered. Last, this study reviewed only those who had received ROP screening or treatment, therefore we were not able to evaluate those who died before being screened.

Conclusions

Retinopathy of prematurity is an important health problem among premature infants in Hong Kong, especially those with ELBW. The results of our study suggest that the current screening service and treatment outcome are satisfactory. Strict adherence to international screening guidelines and vigilance in infants at risk are key to successful ROP management.

Declaration

All authors have disclosed no conflicts of interest.

References

1. Hartnett ME, Penn JS. Mechanisms and management of retinopathy of prematurity. N Engl J Med 2012;367:2515-26.
2. Hartnett ME. Pathophysiology and mechanisms of severe retinopathy of prematurity. Ophthalmology 2015;122:200-10.
3. Hellström A, Smith LE, Dammann O. Retinopathy of prematurity. Lancet 2013;382:1445-57.
4. Kong L, Fry M, Al-Samarraie M, Gilbert C, Steinkuller PG. An update on progress and the changing epidemiology of causes of childhood blindness worldwide. J AAPOS 2012;16:501-7.
5. Furtado JM, Lansingh VC, Carter MJ, et al. Causes of blindness and visual impairment in Latin America. Surv Ophthalmol 2012;57:149-77.
6. Haddad MA, Sei M, Sampaio MW, Kara-José N. Causes of visual impairment in children: a study of 3,210 cases. J Pediatr Ophthalmol Strabismus 2007;44:232-40.
7. Sylvester CL. Retinopathy of prematurity. Semin Ophthalmol 2008;23:318-23.
8. Thomas K, Shah PS, Canning R, Harrison A, Lee SK, Dow KE. Retinopathy of prematurity: Risk factors and variability in Canadian neonatal intensive care units. J Neonatal Perinatal Med 2015;8:207-14.
9. Hadi AM, Hamdy IS. Correlation between risk factors during the neonatal period and appearance of retinopathy of prematurity in preterm infants in neonatal intensive care units in Alexandria, Egypt. Clin Ophthalmol 2013;7:831-7.
10. Wilkinson AR, Haines L, Head K, Fielder AR. UK retinopathy of prematurity guideline. Early Hum Dev 2008;84:71-4.
11. Fierson WM; American Academy of Pediatrics Section on Ophthalmology; American Academy of Ophthalmology; American Association for Pediatric Ophthalmology and Strabismus; American Association of Certified Orthoptists. Screening examination of premature infants for retinopathy of prematurity. Pediatrics 2013;131:189-95.
12. Chamney S, McGrory L, McCall E, et al. Treatment of retinopathy of prematurity in Northern Ireland, 2000-2011: a population-based study. J AAPOS 2015;19:223-7.
13. Painter SL, Wilkinson AR, Desai P, Goldacre MJ, Patel CK. Incidence and treatment of retinopathy of prematurity in England between 1990 and 2011: database study. Br J Ophthalmol 2015;99:807-11.
14. International Committee for the Classification of Retinopathy of Prematurity. The International Classification of Retinopathy of Prematurity revisited. Arch Ophthalmol 2005;123:991-9.
15. Good WV; Early Treatment for Retinopathy of Prematurity Cooperative Group. Final results of the Early Treatment for Retinopathy of Prematurity (ETROP) randomized trial. Trans Am Ophthalmol Soc 2004;102:233-50.
16. Mintz-Hittner HA, Kennedy KA, Chuang AZ; BEAT-ROP Cooperative Group. Efficacy of intravitreal bevacizumab for stage 3+ retinopathy of prematurity. N Engl J Med 2011;364:603-15.
17. Asano MK, Papakostas TD, Palma CV, Skondra D. Visual outcomes of surgery for stage 4 and 5 retinopathy of prematurity. Int Ophthalmol Clin 2014;54:225-37.
18. Yu YS, Kim SJ, Kim SY, Choung HK, Park GH, Heo JW. Lens-sparing vitrectomy for stage 4 and stage 5 retinopathy of prematurity. Korean J Ophthalmol 2006;20:113-7.
19. Shah VA, Yeo CL, Ling YL, Ho LY. Incidence, risk factors of retinopathy of prematurity among very low birth weight infants in Singapore. Ann Acad Med Singapore 2005;34:169-78.
20. Li ML, Hsu SM, Chang YS, et al. Retinopathy of prematurity in southern Taiwan: a 10-year tertiary medical center study. J Formos Med Assoc 2013;112:445-53.
21. Rao KA, Purkayastha J, Hazarika M, Chaitra R, Adith KM. Analysis of prenatal and postnatal risk factors of

retinopathy of prematurity in a tertiary care hospital in South India. Indian J Ophthalmol 2013;61:640-4.
22. van Sorge AJ, Termote JU, Kerkhoff FT, et al. Nationwide inventory of risk factors for retinopathy of prematurity in the Netherlands. J Pediatr 2014;164:494-8.e1.
23. Gonçalves E, Násser LS, Martelli DR, et al. Incidence and risk factors for retinopathy of prematurity in a Brazilian reference service. Sao Paulo Med J 2014;132:85-91.
24. Yau GS, Lee JW, Tam VT, Liu CC, Wong IY. Risk factors for retinopathy of prematurity in extremely preterm Chinese infants. Medicine (Baltimore) 2014;93:e314.
25. Yau GS, Lee JW, Tam VT, Liu CC, Chu BC, Yuen CY. Incidence and risk factors for retinopathy of prematurity in extreme low birth weight Chinese infants. Int Ophthalmol 2015;35:365-73.
26. Xu Y, Zhou X, Zhang Q, et al. Screening for retinopathy of prematurity in China: a neonatal units–based prospective study. Invest Ophthalmol Vis Sci 2013;54:8229-36.
27. Yang CY, Lien R, Yang PH, et al. Analysis of incidence and risk factors of retinopathy of prematurity among very-low-birth-weight infants in North Taiwan. Pediatr Neonatol 2011;52:321-6.
28. Bas AY, Koc E, Dilmen U; ROP Neonatal Study Group. Incidence and severity of retinopathy of prematurity in Turkey. Br J Ophthalmol 2015;99:1311-4.
29. Saldeño YP, Favareto V, Mirpuri J. Prolonged persistent patent ductus arteriosus: potential perdurable anomalies in premature infants. J Perinatol 2012;32:953-8.
30. Jegatheesan P, Ianus V, Buchh B, et al. Increased indomethacin dosing for persistent patent ductus arteriosus in preterm infants: a multicenter, randomized, controlled trial. J Pediatr 2008;153:183-9.