Retinopathy of Prematurity in Neonatal Patients with Birth Weight Greater than 1500 g in Taiwan

Yi-Hsing Chen[1], Rey-In Lien[2], Chi-Chun Lai[1], An-Ning Chao[1], Kuan-Jen Chen[1], Yih-Shiou Hwang[1], Nan-Kai Wang[1], Yen-Po Chen[1], Tun-Lu Chen[1], Chee-Jen Chang[3,4], Wei-Chi Wu[1]

Background: To understand the characteristics, ophthalmic outcomes, and risk factors of retinopathy of prematurity (ROP) in patients with birth weight (BW) greater than 1500 g. The applicability of the ROP screening criteria to the Taiwanese population was also examined.

Methods: The study included 104 eyes from 54 ROP patients who had BW greater than 1500 g from 1981 to 2008. Demographic information, disease courses, ophthalmic outcomes, and possible systemic risk factors were recorded. The infants were divided into groups of mild and severe ROP for a risk factor analysis.

Results: The mean gestational age (GA) of the infants was 31 ± 1.3 weeks, and the mean BW was 1675 ± 249 g. Mild ROP regressed in 94 eyes (90%), and 10 eyes (10%) developed severe ROP. After various treatments, the regression rates for prethreshold or threshold ROP ($n = 8$) and stage 4 ROP ($n = 2$) were 100% and 50%, respectively. Forty-eight patients (85%) had at least three associated systemic risk factors. A multiple logistic regression analysis revealed that patients with an intraventricular hemorrhage were found to have an increased chance of developing severe ROP, especially those with BW greater than 1500 g ($p = 0.015$). There was also a significant association between patients who had severe ROP and an increased risk of having cerebral palsy (CP) at 1.5 years of age ($p = 0.013$).

Conclusion: The majority of patients with BW greater than 1500 g developed mild ROP. However, advanced ROP with poor visual outcome was also encountered in some patients.
(Biomed J 2013;36:84-89)

Key words: birth weight, cerebral palsy, retinopathy of prematurity

At a Glance Commentary

Scientific background of the subject

Retinopathy of prematurity (ROP) usually occurs in infants with lower birth weight and lower gestational age. The current paper discuss the characteristics and risk factors associated with ROP in higher BW infants.

What this study adds to the field

Although most patients in this birth weight group develop minor ROP that required no treatment, the current study discovered that 10% of the babies with birth weight more than 1500 g developed severe ROP that required treatment.

Retinopathy of prematurity (ROP) is a vision-threatening disorder that generally occurs in babies with very low birth weight (BW). As technology has advanced, more premature infants have survived. Over the years, progress has been made on how we screen for, record, and treat ROP patients.[1-6] However, some aspects of ROP remain unknown and need to be further explored.

In general, ROP develops more frequently in preterm infants with lower BW.[7] However, it has been reported that some "higher BW" infants develop ROP. Hutchinson, *et al*., found that 7 out of 697 infants with BW greater than 1500 g had ROP requiring treatment.[8] Yanovitch *et al*., identified

From the [1]Departments of Ophthalmology, Chang Gung Memorial Hospital at Linkou, Chang Gung University College of Medicine, Taoyuan, Taiwan, [2]Department of Pediatrics, Chang Gung Memorial Hospital at Linkou, Chang Gung University College of Medicine, Taoyuan, Taiwan, [3]Biostatistical Center for Clinical Research, Chang Gung Memorial Hospital at Linkou, Chang Gung University College of Medicine, Taoyuan, Taiwan, [4]Graduate Institute of Clinical Medical Science and Clinical Informatics and Medical Statistics Research Center, Chang Gung University, Taoyuan, Taiwan
Received: May 29, 2012; Accepted: Jul. 4, 2012
Correspondence to: Dr. Wei-Chi Wu, Department of Ophthalmology, Chang Gung Memorial Hospital at Linkou. 5, Fusing St., Gueishan, Taoyuan 333, Taiwan (R.O.C.). Tel: 886-3-3281200 ext. 8666; Fax: 886-3-3287798; E-mail: weichi666@gmail.com

DOI: 10.4103/2319-4170.110399

mild ROP in 4 of 111 babies with BW greater than 1500 g.[9] Although several studies have reported the clinical features of this particular group of patients, information related to severe ROP remains sparse.[10,11] The aims of the present study are to investigate the characteristics; the ophthalmic outcomes, and the risk factors leading to ROP in babies with BW greater than 1500 g. This study also examines the relevance of contemporary ROP screening criteria in Taiwanese pediatric population.

METHODS

A retrospective study was performed in our hospital between January 1981 and December 2008. Infants born with BW between 1500 and 2000 g; gestational age (GA) less than 35 weeks or BW greater than 2000 g, but without stable clinical courses, especially those requiring cardiopulmonary support or having sepsis were routinely screened for ROP. Infants with detailed hospital records and a follow-up period of greater than 3 months were included. The patients were first screened at 4-6 weeks of postnatal age and were examined regularly every 1-2 weeks until complete vascularization of the retina. Some patients received further ophthalmic check-up after 3 years of age. Those without complete medical records, follow-up duration less than 3 months, or those referred from other hospitals but failed to have the first screening at 4-6 weeks of postnatal age were all excluded. This study was performed under the approval of the Institutional Review Board of Chang Gung Memorial Hospital, Taoyuan, Taiwan (99-0418B).

Patients' demographic information, including BW, GA, sex, medical histories, ROP severity, treatment course, and outcome, were recorded. Patients with mild ROP did not receive any interventions during the follow-up period, whereas patients with prethreshold or threshold ROP were treated with peripheral cryotherapy or laser ablation according to the timings suggested by the Cryotherapy for Retinopathy of Prematurity (CRYO-ROP)[3] and the Early Treatment for Retinopathy of Prematurity (ETROP) studies.[5] Patients with retinal detachment were treated with vitrectomy and/or scleral buckle. Cycloplegic refraction and the best-corrected vision with a standard Snellen chart were measured in patients when they could cooperate with the testing. The presence of cerebral palsy (CP), as diagnosed by a pediatric neurologist, at the age of 1.5 years was particularly noted to examine its relationship with the severity of ROP.

Some systemic risk factors that have been found potentially associated with the development of ROP including bronchopulmonary dysplasia, intraventricular hemorrhage (IVH), necrotizing enterocolitis, patent ductus arteriosus, respiratory distress syndrome, sepsis, pneumonia, anemia, apnea of prematurity, the use of surfactant, and assisted ventilation were recorded.[12-16] Possible maternal risk factors including delivery type (vaginal delivery or cesarean section), premature rupture of the membrane, chorioamnionitis, and multiple births were also recorded.[12-16] Treatment outcomes and systemic risk factors were analyzed and compared between patients with severe ROP (prethreshold, threshold, or stage 4 ROP) and patients with mild ROP (stage 1, stage 2).

The following contemporary screening criteria were used to examine the applicability to ROP patients with BW greater than 1500 g in Taiwan. The criteria established by the American Academy of Pediatrics in 2001 suggested that ROP screening be conducted on infants with BW less than 1500 g, GA less than 28 weeks, or BW between 1500 and 2000 g but coupled with an unstable clinical course as defined by their pediatricians.[17] The recent criteria from the American Academy of Pediatrics updated in 2006 broadened the screening cut-off to infants who had BW less than 1500 g or GA of 32 weeks or less or infants who had BW between 1500 and 2000 g or GA greater than 32 weeks but associated with an unstable clinical course, especially infants who required cardio-respiratory support.[18] Local criteria proposed by Fang, *et al*., in 2006 suggested that infants with GA less than 34 weeks or BW less than 1600 g be screened.[19] Another set of local criteria proposed by Chiang *et al*., in 2002 suggested that infants with BW less than 1500 g or GA less than 31 weeks be screened, but their clinical course was not mentioned.[20]

Fisher's exact test was used to analyze the categorical data, and Mann–Whitney test was used to compare the numerical data. Univariate logistic regression was used to examine the prognostic factors that are related to unfavorable outcome of ROP. The odds ratios (OR) and the 95% confidence intervals of the OR are presented. A stepwise multiple logistic regression with forward elimination was used to further evaluate the interactions among possible risk factors. Statistical analyses were performed using the SPSS software package (version 12.0 for Windows, SPSS Inc., Chicago, IL, USA). A two-tailed p value of 0.05 or less was considered significant for all tests.

RESULTS

Between 1981 and 2008, 104 eyes of 54 patients (37 males and 17 females) with BW greater than 1500 g who had developed ROP were included in this study. The mean BW of these patients was 1675 ± 249 g (range 1500-3060 g). The mean GA of these infants was 31 ± 1.3 weeks (range 27-34 weeks). The average age of the mothers was 30 years (range 16-40 years). The mean duration of the follow-up period was 22 months (range 3-96 months). Sixteen patients (30%) had a follow-up duration of more than 18 months. The patients' demographic data are presented in Table 1.

Among all of the ROP eyes, 81 (78%), 13 (12%), 8 (8%),

Table 1: Outcomes of patients with retinopathy of prematurity and birth weights greater than 1500 g

Stage	1	2	3	4
Number of patients (eyes)	41 (81)	7 (13)	4 (8)	2 (2)
BW (g) (mean±SD, range)	1671±248, 1500-3060	1669±98, 1500-1800	1811±468, 1530-2510	1525±35, 1500-1550
GA (weeks) (mean±SD, range)	31±1.2, 29-33	31±1.2, 30-34	32±1.7, 29-32	29±2.1, 27-30
Treatments (eyes)	None	None	Cryotherapy (4) Laser (4)	Vitrectomy (1) Buckle (1)
Regression of ROP (%)	100	100	100	50

Abbreviations: BW: Birth weight; GA: Gestational age; SD: Standard deviation

and 2 eyes (2%) developed stage 1, 2, 3, and 4 ROP, respectively. Fifty patients (93%) had bilateral involvement. Mild ROP that only required observation was found in 94 eyes (90%), and 10 eyes (10%) developed more severe ROP that required treatment. Of the 10 eyes with prethreshold or threshold ROP, 6 eyes received laser treatment and the other 4 eyes had cryotherapy. Eight eyes with threshold or prethreshold ROP responded favorably to these peripheral retinal ablative procedures and exhibited complete regression of ROP. Among these eight eyes, two were complicated by vitreous hemorrhage after cryotherapy and one developed macular dragging. Two eyes progressed to stage 4A despite laser treatment for prethreshold ROP. One eye improved after additional scleral buckle and vitrectomy. The patient had complications like dragging of the optic disc and the macula. The other eye with stage 4 ROP did not receive further surgical intervention due to familial refusal, and the lack of surgical intervention resulted in total detachment of the retina.

The best-corrected visual acuities of 8 patients (16 eyes) and the cycloplegic refraction results of 12 patients (24 eyes) were available at the mean age of 5.1 years (range 3-8 years) [Figure 1]. The refraction data consisted of nine mild ROP patients (75%) and three severe ROP patients (25%). The best-corrected visual acuities in this cohort study were as follows: Nine eyes (56%) achieved 20/20 or better vision; four eyes (25%) had visual acuities less than 20/20, but better than or equal to 20/40; one eye (6%) had a visual acuity less than 20/40, but better than or equal to 20/200; and only two eyes (13%) had vision worse than 20/200. The average spherical equivalent of the eyes was +0.73 diopters (D) (range −1.00 to +4.00 D). Seventeen eyes (71%) developed mild hyperopia (≧0 D and <3 D), three eyes (12%) developed high hyperopia (≧3 D), four eyes (17%) developed mild myopia (≧−3 D and <0 D), and none of the eyes had high myopia (<−3 D). Two eyes (8%) developed significant astigmatism (≧2.5 D).

At 1.5 years of age, 16 patients were evaluated by a pediatric neurologist and CP was diagnosed in 1 of 11 patients (9%) with mild ROP and in 4 of 5 patients (80%) with severe ROP. The incidence of CP was statistically higher in patients with severe ROP (univariate logistic regression, OR = 40.0, 95% CI of OR: 2-807, $p = 0.013$).

Table 2: Risk factors in patients with mild and severe retinopathy of prematurity

Risk factors	Mild ROP (n=48) n (%) or Mean±SD	Severe ROP (n=6) n (%) or Mean±SD	p value
GA	31.1±1.2	29.8±1.9	0.028
Number of risk factors	4.1±1.8	5.8±1.5	0.030
IVH	8 (16.7)	4 (66.7)	0.018
PDA	7 (14.6)	3 (50)	0.070
RDS	37 (77.1)	4 (66.7)	0.623
NEC	2 (4.2)	0 (0.0)	1.000
BPD	6 (12.5)	1 (16.7)	1.000
Sepsis	23 (47.9)	3 (50.0)	1.000
Pneumonia	11 (22.9)	1 (16.7)	1.000
Anemia	23 (47.9)	3 (50.0)	1.000
Apnea of prematurity	11 (22.9)	0 (0.0)	0.327
Surfactant usage	11 (22.9)	2 (33.3)	0.623
Vaginal delivery	16 (33.3)	3 (50.0)	0.336
Multiple births	13 (27.1)	0 (0.0)	0.317
PROM	15 (31.9)	0 (0.0)	0.307
Chorioamnionitis	3 (6.4)	0 (0.0)	1.000

Abbreviations: BPD: Bronchopulmonary dysplasia; GA: Gestational age; IVH: Intraventricular hemorrhage; NEC: Necrotizing enterocolitis; PDA: Patent ductus arteriosus; PROM: Premature rupture of membranes; ROP: Retinopathy of prematurity; RDS: Respiratory distress syndrome

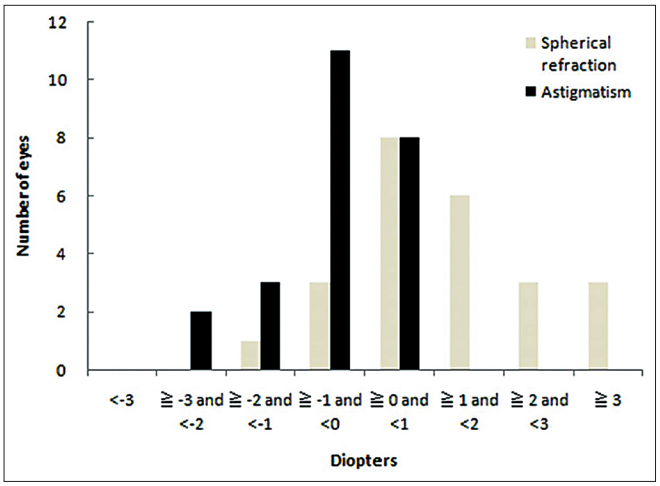

Figure 1: The refraction status of ROP patients with BW greater than 1500 g. Most of the patients had mild hyperopia at 3 years of age

The potential systemic and maternal risk factors were compared between the infants with mild and severe ROP. The results are shown in Table 2. All 54 infants (100%) had at least one associated risk factor, 51 patients (94%) had at least

two associated risk factors, and 48 patients (89%) had at least three associated risk factors. A univariate logistic regression analysis revealed that the number of risk factors (OR = 1.8, 95% CI of OR: 1.0-3.1, $p = 0.041$), GA (OR = 0.5, 95% CI of OR: 0.2-1.0, $p = 0.044$) and the presence of IVH (OR = 10.0, 95% CI of OR: 1.6-64.2, $p = 0.018$) were significantly different between infants with mild and severe ROP. These results are shown in Table 3. However, after a stepwise multiple logistic regression with forward elimination, only IVH remained as a significant risk factor for the development of severe ROP (regression coefficient 2.30, OR = 10.0, 95% CI of OR: 1.6-64.2, $p = 0.015$).

We examined the applicability of the two criteria proposed by the American Academy of Pediatrics and the two criteria proposed by local researchers to infants with BW greater than 1500 g in the current study. Using the criteria that were published by the American Academy of Pediatrics in 2001,[17] we would have missed two patients (3.7%) who eventually developed ROP. Using the updated guidelines from the American Academy of Pediatrics in 2006[18] or Fang's criteria,[19] all patients would have been appropriately diagnosed. If we had adopted the criteria proposed by Chiang *et al.*,[20] we would have missed a total of 18 patients (33%), including 2 patients (11%) who developed severe ROP that required treatment.

Table 3: Univariate analysis of the association between risk factors and severe retinopathy of prematurity requiring treatment

Parameter	No./Total (%) or Regression coefficient (SE)	OR	95% CI of OR	*p* value
IVH				
Observation needed ROP	8/48 (16.7)	10.0	1.6-64.2	0.018
Treatment needed ROP	4/6 (66.7)			
GA	0.75 (0.37)	0.5	0.2-1.0	0.044
Number of risk factors	0.59 (0.29)	1.8	1.0-3.1	0.041

Abbreviations: CI: Confidence interval; GA: Gestational age; IVH: Intraventricular hemorrhage; OR: Odds ratio; ROP: Retinopathy of prematurity; SE: Standard error associated with the coefficient

DISCUSSION

With this study, we reaffirmed the previous reports that ROP can still develop in babies with BW greater than 1500 g [Table 4].[8-10,21,22] Our study shows that all the patients have at least one associated systemic risk factor. The majority of these higher BW patients only developed mild ROP and did not require any treatment. Hutchinson *et al.* and Yanovitch *et al.*, reported similar results.[8,9] However, severe ROP that required treatment was still encountered in 10% of the eyes in this study. Fielder reported that 54% of the infants who required treatment for ROP had BW greater than 1500 g in Lithuania and Hungary.[23] Previous studies found that GA and BW are the strongest predictors of the development of ROP in low BW infants. Our study discovered that IVH is the most significant factor associated with the development of severe ROP that requires treatment in infants with BW greater than 1500 g. The patients who had severe ROP were also found to have a higher incidence of CP at 1.5 years of age ($p = 0.013$). The average spherical equivalent of the patients in the present study at the mean age of 5.1 years was slightly hyperopic.

Previous studies have shown that the development of ROP with BW greater than 1250 g only occurred in infants with two or more significant risk factors, including more than 96 h of mechanical ventilation, sepsis, more than 14 days of antibiotic treatment, more than 7 units of transfused red blood cells, central line placement, respiratory distress syndrome, or multiple births.[9-11] All of our patients had at least one associated risk factor, and 94% of the babies in this study had at least two associated risk factors. After a stepwise analysis using multiple logistic regressions, IVH was found to be the only predictor of ROP that required treatment. Similar results have been found in other studies.[9,22]

CP, a major neurodevelopmental impairment that is generally diagnosed in late childhood, is frequently associated with low BW and IVH.[24,25] The association between CP and ROP has been reported in some studies of children who had very low BW.[26,27] Schmidt *et al.*, discovered that severe ROP has an independent significant influence ($p < 0.01$) and an add-on OR of 2.9 (95% CI of OR: 2.4-3.5) in the development of CP in infants who had extremely low BW.[27]

Table 4: Studies of retinopathy of prematurity in premature infants with birth weights greater than 1500 g

Author	Year published	Study duration	Number of ROP patients with BWs > 1500 g	Incidence of ROP requiring treatment	Stage 4 or 5 ROP
Yang *et al.*[18]	2001	1997-1998	4	NA	NA
Hutchinson *et al.*[8]	2003	1993-1999	70	10%	0%
Al-Essa *et al.*[10]	2003	1996-1997	13	0%	0%
Yanovitch *et al.*[9]	2006	2001-2004	4	0%	0%
Gu *et al.*[17]	2011	2005-2008	54	7.4%	0%
Current study	2012	1981-2008	54	10%	2%

Abbreviations: BW: Birth weight; NA: Not available; ROP: Retinopathy of prematurity

However, a relationship between CP and ROP in higher BW infants has never been reported. In the particular group of patients that we studied, the incidence of CP was higher in patients who had severe ROP than in patients with mild ROP (OR = 40.0, 95% CI of OR: 2-807, $p = 0.013$). Of note, only 16 patients (30%) were evaluated for CP by pediatricians due to loss to follow-up of the other patients. Further study is needed to confirm this finding.

Despite modern neonatal intensive care and better use of oxygen for premature infants, ROP still occurred in higher BW infants. Although ROP is most often related to a lower BW and a younger GA,[6,28,29] these factors do not necessarily predict the severity of ROP in higher BW infants. Other factors, such as genetic susceptibility, have also been found that can account for the development of ROP. Abnormalities in the Wnt signaling pathway during retinal development, including the Norrie disease (ND) gene, the *FZD4* gene, and the *LRP5* gene, may contribute to the development of severe ROP.[30-33] Higher BW infants who develop ROP may have some genetic alterations that result in the development of the disease. Further study is required to determine the role of genetics.

Differences in ethnicity, race, and the standard of care for ROP may account for differences in the incidence of ROP among different countries. Therefore, each country should develop suitable domestic screening criteria for ROP. Of the four sets of criteria that have been described above, the screening criteria that were proposed by the American Academy of Pediatrics in 2006[18] and by Fang's group in 2006[19] would not have excluded any of the infants who developed ROP in this study. To date, however, no clear definitions regarding what constitutes an "unstable clinical course" have been established, and it is judged by the pediatricians. This could lead to different screening criteria and ultimately result in different screening volumes for ophthalmologists. Additional studies aimed at establishing a clearer definition of an "unstable clinical course" are needed to provide a better guideline for clinicians.

The limitations of this study include its retrospective design, small sample size, lack of a control group, and the variable duration of the follow-up period among the patients. In addition, visual acuity data were not available for every patient. However, some useful information could still be gleaned from this study. Although the majority of patients in this study developed mild ROP with no need for treatment, we found that severe ROP requiring treatment could still occur in higher BW neonates provided that they had multiple systemic risk factors. The infants who had IVH were likely to develop severe ROP, especially the patients with BW greater than 1500 g. These patients might have a higher incidence for the development of CP in the future.

In conclusion, it is worthwhile to screen premature infants, even whose BW is greater than 1500 g, especially when there are associated unstable clinical courses. Most cases of ROP in this group of patients are likely to regress. However, our study also reveals that when the infants present with IVH, they have a higher possibility of developing severe ROP requiring treatment. Severe ROP patients were found to have a higher incidence of CP at 1.5 years of age ($p = 0.013$). Further genetic study may elucidate the underlying pathogenesis of ROP in these higher BW infants.

REFERENCES

1. Reynolds JD, Dobson V, Quinn GE, Fielder AR, Palmer EA, Saunders RA, *et al*. Evidence-based screening criteria for retinopathy of prematurity: Natural history data from the CRYO-ROP and LIGHT-ROP studies. Arch Ophthalmol 2002;120:1470-6.
2. An international classification of retinopathy of prematurity. II. The classification of retinal detachment. The international committee for the classification of the late stages of retinopathy of prematurity. Arch Ophthalmol 1987;105:906-12.
3. Hardy RJ, Palmer EA, Schaffer DB, Phelps DL, Davis BR, Cooper CJ. Outcome-based management of retinopathy of prematurity. Multicenter trial of cryotherapy for retinopathy of prematurity cooperative group. J AAPOS 1997;1:46-54.
4. An international classification of retinopathy of prematurity. The committee for the classification of retinopathy of prematurity. Arch Ophthalmol 1984;102:1130-4.
5. Early treatment for retinopathy of prematurity cooperative group. Revised indications for the treatment of retinopathy of prematurity: Results of the early treatment for retinopathy of prematurity randomized trial. Arch Ophthalmol 2003;121:1684-94.
6. Schaffer DB, Palmer EA, Plotsky DF, Metz HS, Flynn JT, Tung B, *et al*. Prognostic factors in the natural course of retinopathy of prematurity. The cryotherapy for retinopathy of prematurity cooperative group. Ophthalmology 1993;100:230-7.
7. Todd DA, Smith J. Incidence and treatment of severe retinopathy of prematurity. Arch Dis Child Fetal Neonatal Ed 2009;94:F467.
8. Hutchinson AK, O'Neil JW, Morgan EN, Cervenak MA, Saunders RA. Retinopathy of prematurity in infants with birth weights greater than 1250 grams. J AAPOS 2003;7:190-4.
9. Yanovitch TL, Siatkowski RM, McCaffree M, Corff KE. Retinopathy of prematurity in infants with birth weight ≥ 1250 grams-incidence, severity, and screening guideline cost-analysis. J AAPOS 2006;10:128-34.
10. Al-Essa M, Rashwan N, Al-Ajmi M. Retinopathy of prematurity in infants with birth weight above 1500 grams. East Afr Med J 2000;77:562-4.
11. Jandeck C, Kellner U, Kossel H, Bartsch M, Versmold HT, Foerster MH. Retinopathy of prematurity in infants of birth weight > 2000 g after haemorrhagic shock at birth. Br J Ophthalmol 1996;80:728-31.
12. Seiberth V, Linderkamp O. Risk factors in retinopathy of prematurity. A multivariate statistical analysis. Ophthalmologica 2000;214:131-5.
13. Akkoyun I, Oto S, Yilmaz G, Gurakan B, Tarcan A, Anuk D, *et al*. Risk factors in the development of mild and severe retinopathy of prematurity. J AAPOS 2006;10:449-53.

14. Wu WC, Ong FS, Kuo JZ, Lai CC, Wang NC, Chen KJ, *et al*. Retinopathy of prematurity and maternal age. Retina 2010;30:327-31.

15. Recchia FM, Capone A Jr. Contemporary understanding and management of retinopathy of prematurity. Retina 2004;24:283-92.

16. O'Connor AR, Stephenson T, Johnson A, Tobin MJ, Moseley MJ, Ratib S, *et al*. Long-term ophthalmic outcome of low birth weight children with and without retinopathy of prematurity. Pediatrics 2002;109:12-8.

17. American Academy of Pediatrics. Section on Ophthalmology. Screening examination of premature infants for retinopathy of prematurity. Pediatrics 2001;108:809-11.

18. Section on Ophthalmology American Academy of Pediatrics; American Academy of Ophthalmology; American Association for Pediatric Ophthalmology and Strabismus. Screening examination of premature infants for retinopathy of prematurity. Pediatrics 2006;117:572-6.

19. Fang PC, Kuo HK, Ko TY, Chen CC, Hwang KP, Chung MY. Retinopathy of prematurity in larger preterm infants. Am J Perinatol 2006;23:273-7.

20. Chiang MC, Tang JR, Yau KI, Yang CM. A proposal of screening guideline for retinopathy of prematurity in Taiwan. Acta Paediatr Taiwan 2002;43:204-7.

21. Gu MH, Jin J, Yuan TM, Yu HM. Risk factors and outcomes for retinopathy of prematurity in neonatal infants with a birth weight of 1,501-2,000 g in a Chinese Neonatal Unit. Med Princ Pract 2011;20:244-7.

22. Yang CS, Chen SJ, Lee FL, Hsu WM, Liu JH. Retinopathy of prematurity: Screening, incidence and risk factors analysis. Zhonghua Yi Xue Za Zhi (Taipei) 2001;64:706-12.

23. Fielder AR. The impact of low birth weight on the visual pathway. Br J Ophthalmol 1998;82:1-2.

24. Futagi Y, Toribe Y, Ogawa K, Suzuki Y. Neurodevelopmental outcome in children with intraventricular hemorrhage. Pediatr Neurol 2006;34:219-24.

25. Msall ME. The panorama of cerebral palsy after very and extremely preterm birth: Evidence and challenges. Clin Perinatol 2006;33:269-84.

26. Sugimoto S, Furukawa A, Hatsukawa Y, Yanagihara K, Saito Y. Weak association between retinopathy of prematurity and neurological disorders in childhood. Jpn J Ophthalmol 1998;42:142-5.

27. Schmidt B, Asztalos EV, Roberts RS, Robertson CM, Sauve RS, Whitfield MF. Impact of bronchopulmonary dysplasia, brain injury, and severe retinopathy on the outcome of extremely low-birth-weight infants at 18 months: Results from the trial of indomethacin prophylaxis in preterms. JAMA 2003;289:1124-9.

28. Fielder AR, Shaw DE, Robinson J, Ng YK. Natural history of retinopathy of prematurity: A prospective study. Eye (Lond) 1992;6 (Pt 3):233-42.

29. Wright K, Anderson ME, Walker E, Lorch V. Should fewer premature infants be screened for retinopathy of prematurity in the managed care era? Pediatrics 1998;102:31-4.

30. Drenser KA, Dailey W, Vinekar A, Dalal K, Capone A, Jr., Trese MT. Clinical presentation and genetic correlation of patients with mutations affecting the FZD4 gene. Arch Ophthalmol 2009;127:1649-54.

31. Haider MZ, Devarajan LV, Al-Essa M, Kumar H. A C597->A polymorphism in the Norrie disease gene is associated with advanced retinopathy of prematurity in premature Kuwaiti infants. J Biomed Sci 2002;9:365-70.

32. Hiraoka -M, Takahashi H, Orimo H, Hiraoka M, Ogata T, Azuma N. Genetic screening of Wnt signaling factors in advanced retinopathy of prematurity. Mol Vis 2010;16:2572-7.

33. Mandal K, Drury JA, Clark DI. An unusual case of retinopathy of prematurity. J Perinatol 2007;27:315-6.