Original Article

Retinopathy of Prematurity in 5 Neonatal Units at the 7th Health District of Thailand

Pongsatorn Paopongsawan MD[1], Junya Jirapradittha MD[1], Pakaphan Kiatchoosakun MD[1], Pantipa Wongwai MD[2]

[1] Division of Neonatology, Department of Pediatrics, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand
[2] Division of Pediatric Ophthalmology, Department of Ophthalmology, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand

Objective: To study the incidence of retinopathy of prematurity [ROP] and factors associated with ROP at 5 different hospitals in the 7th health region of Thailand and to propose ROP screening criteria with higher sensitivity for ROP detection suitable for the region.

Materials and Methods: A retrospective descriptive study conducted by reviewing the results of screening eye examinations of 662 infants obtained from the included hospitals during October 2013 to September 2014.

Results: From the present study, 338 infants (58.6%) were males with mean birth weight of 1,604±525 grams and mean gestational age of 31.8±2.9 weeks. The regional overall rate of ROP was 31.7% and ROP rate was statistically significant higher in infants with birth weight less than 1,500 grams (46.8% vs. 19.1%, $p<0.001$) and gestational age less than 32 weeks (47.0% vs. 20.7%, $p<0.001$). The hospital where the infant admitted was also a significant factor, while the survival rate was not statistically significant associated with rate of ROP. Suggested criteria for ROP screening eye examination were infants with birth weight less than 1,935 grams or gestational age less than 34 weeks which would have sensitivity for ROP detection at 90.0% and 91.4%, respectively.

Conclusion: The rate of ROP was different among hospitals which could be related to different practices in neonatal care and should be studied furthermore. Criteria for screening eye examination should be adjusted for each hospital to improve the sensitivity for ROP detection with appropriate ophthalmologists' workload.

Keywords: Retinopathy of prematurity, ROP, Risk factors, Criteria, ROP screening, Different hospital

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Retinopathy of prematurity [ROP] is an important cause of blindness in neonates and infants worldwide, especially in preterm infants[1-4]. Multiple factors can affect the rate and severity of ROP including oxygen toxicity[5,6], prematurity, low birth weight[1,2], and mortality rate[7]. For prevention, ROP screening eye examination is suggested in infants with birth weight less than 1,500 grams and gestational age less than 32 weeks[8]. Since preterm infants in developed countries have higher survival rate and lower incidence of ROP than in developing countries[9], therefore using ROP screening criteria established by developed countries[8,10,11], which has been practicing in Thailand, might not be appropriate and some infants with ROP can be undetected. Neonatal care practices and mortality rate are also different among hospitals and can lead to different rate of ROP. Thus, individualized criteria for ROP screening based on local hospital data should be applied[12,13].

The objectives of the present study were to determine the incidence of ROP among 5 hospitals in the 7th health district of Thailand, as well as factors associated and to propose an individualized ROP screening criteria for each hospital.

Materials and Methods

The present study was a retrospective descriptive study conducted by reviewing the results of ROP screening examined by a single pediatric ophthalmologist between October 2013 and September 2014. The data were collected from 5 hospitals in the 7th health district which comprised of 4 provinces in the North-eastern part of Thailand. Each hospital had different level of neonatal unit categorized by the British Association of Perinatal Medicine[14] and different practices of neonatal care. The ROP screening examination in each hospital was performed according to the American Academy of Pediatrics [AAP] 2006 screening examination of premature infants for ROP guideline[8]. The present study used

Correspondence to:

Jirapradittha J. Department of Pediatrics, Faculty of Medicine, Khon Kaen University, Khon Kaen 40002, Thailand.
Phone: +66-43-363012, **Fax**: +66-43-348382
Email: jjirapradittha@yahoo.com

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the AAP 2006 guideline instead of the more recent 2013 version because the 2006 guideline was widely used by pediatricians in the region prior to the study period. Also, preterm infants survival rate in Thailand was much lower than in the United States of America leading to more cases would be missing the ROP screening examination if using the 2013 guideline. According to Lai et al study[15] which also used the AAP 2006 criteria showed that the incidence of ROP among infants in Taiwan was 38.7% thus the sample size required for the present study based on this data was 365 infants. The data collected for the present study were focused on general demography, gestational age, birth weight, age of the infant when first ROP screening examination was performed, number of ROP screening examination, severity of ROP and treatments of ROP. The severity of ROP in the present study was furthermore categorized into mild ROP requiring follow-up eye examination, and severe ROP requiring treatments to prevent disease progression. The data also included hospital characteristics which were: birth rate, mortality rate and the level of neonatal unit.

Statistical analysis was performed using SPSS version 19.0. Percent, mean ± SD, and median with interquartile range were used to present descriptive data. Association analysis was performed by using Chi-square test or Fisher's exact test. Comparative analysis was performed by using Student t-test or Mann-Whitney U-test. A receiver operating characteristic [ROC] curve was used to calculate the cut point for the proposal ROP screening criteria and p-value <0.05 was considered statistically significant. The present study was approved by the Ethics Committee for Human Research of Khon Kaen University.

Results

During the study period, eye examination data records of 703 infants from 5 hospitals, named hospital A, B, C, D, and E, were collected. Of these, 41 infants were excluded due to incomplete data records which resulted in 662 eligible infants for the study.

For each hospital, there was no statistically significant difference in total survival rate, but the survival rate of infants with birth weight less than 1,500 grams and gestational age less than 32 weeks was statistically significant different as hospital A had the highest survival rate. The level of neonatal unit among hospitals were also different with statistically significance. Each hospital characteristics were shown in Table 1.

The demographic data of 662 infants presented in Table 2 showed statistically significant differences

Table 1. Description of hospital characteristics

Hospital	A	B	C	D	E	*p*-value
Type	Teaching university	Regional referral	Tertiary	Tertiary	Tertiary	-
Level-2 neonatal unit (No.)	1	2	1	1	1	-
Level-3 neonatal unit (No.)	1	1	0	0	0	-
Total live birth	2,345	5,987	3,322	3,775	4,581	0.283
Total survival rate (%)	97.9	98.9	99.1	99.1	99.0	0.406
BW <1,500 g survival rate (%)	89.8	50.7	76.8	55.0	41.5	0.002
GA <32 weeks survival rate (%)	84.5	68.7	78.5	58.2	43.7	0.001

BW = birth weight; GA = gestational age

Table 2. Characteristics of infants included in the present study

Hospital	A	B	C	D	E	Total	*p*-value
Cases, n (%)	122 (18.4)	229 (34.6)	121 (18.3)	72 (10.9)	118 (17.8)	662 (100)	0.891
Male, n (%)	74 (60.6)	135 (58.9)	73 (60.3)	39 (54.1)	67 (56.7)	388 (58.6)	0.743
BW (g), mean ± SD	1,544±620	1,630±522	1,664±534	1,539±333	1,595±505	1,604±525	0.098
GA (week), mean ± SD	31.4±2.9	32.2±2.7	32.3±3.2	31.9±2.7	31.2±2.9	31.9±2.9	0.004
BW <1,500 g, n (%)	68 (55.7)	103 (44.9)	44 (36.4)	29 (40.3)	57 (48.3)	301 (45.5)	0.749
GA <32 weeks, n (%)	64 (52.4)	80 (34.9)	47 (38.8)	31 (43.0)	63 (53.4)	285 (43.1)	0.445
Admission, n (%)							<0.001
Level-2 neonatal unit	15 (12.3)	89 (38.9)	121 (100)	72 (100)	118 (100)	415 (62.7)	
Level-3 neonatal unit	107 (87.7)	140 (61.1)	0 (0.0)	0 (0.0)	0 (0.0)	247 (37.3)	

BW = birth weight; GA = gestational age

Table 3. Results of ROP screening examination

Hospital	A	B	C	D	E	Total	*p*-value
No. of total cases, n (%)							
No ROP	101 (82.8)	159 (69.4)	95 (78.5)	56 (77.8)	41 (34.7)	452 (68.3)	<0.001
Mild ROP	10 (8.2)	44 (19.3)	20 (16.5)	10 (13.9)	38 (32.2)	122 (18.4)	<0.001
Severe ROP	11 (9.0)	26 (11.3)	6 (5.0)	6 (8.3)	39 (33.1)	88 (13.3)	<0.001
BW <1,500 g, n (%)							
No ROP	51 (75.0)	53 (51.5)	29 (65.9)	19 (65.5)	8 (14.0)	160 (53.2)	<0.001
Mild ROP	9 (13.2)	28 (27.2)	11 (25.0)	6 (20.7)	24 (42.1)	78 (25.9)	<0.001
Severe ROP	8 (11.8)	22 (21.4)	4 (9.1)	4 (13.8)	25 (43.9)	63 (20.9)	<0.001
GA <32 weeks, n (%)							
No ROP	48 (75.0)	41 (51.3)	32 (68.1)	20 (64.5)	10 (15.9)	151 (53.0)	<0.001
Mild ROP	9 (14.1)	22 (27.5)	11 (23.4)	6 (19.4)	26 (41.3)	74 (26.0)	<0.001
Severe ROP	7 (10.9)	17 (21.3)	4 (8.5)	5 (16.1)	27 (42.9)	60 (21.1)	<0.001

ROP = retinopathy of prematurity; BW = birth weight; GA = gestational age

in gestational age and the level of neonatal unit where the infants admitted among the hospitals included in the present study. However, there were no statistically significant differences in birth weight, sex, number of infants with birth weight less than 1,500 grams and number of infants with gestational age less than 32 weeks.

The overall average ROP rate was 31.7%. Among the infants with ROP, 18.4% had mild ROP while 13.3% had severe ROP. Hospital A, B, C, and D had ROP rate lower than average. Hospital E had the highest ROP rate at 65.2%, while hospital A had the lowest ROP rate at 17.2%. In infants with birth weight less than 1,500 grams and gestational age less than 32 weeks, the average ROP rate were 46.8% and 47.0%, respectively, with hospital E had the highest ROP rate of both groups at 85.9% and 84.1%. Most infants only required follow-up eye examination, but 13.3% required further treatments which included laser indirect ophthalmoscopy, intravitreous injection of vascular endothelial growth factor inhibitor and pars plana vitrectomy. Table 3 showed the results of ROP screening examination of each hospital.

From the present study, risk factors significantly associated with ROP were infants with birth weight less than 1,500 grams and gestational age less than 32 weeks. Admission hospital was also associated with different risk of ROP. Statistically significant reduction in the risk of ROP was observed in infants admitted to hospital A and C, while admission to hospital E increased the risk of ROP. The risk of ROP in infants admitted to hospital B and D were not statistically significant. The risk of ROP in infants with birth weight less than 1,500 grams and gestational age less than 32 weeks admitted to hospital A and C was also reduced. The list of risk factors associated with ROP was shown in Table 4.

Table 4. Risk factors associated with ROP

Factors	Odds ratio	95% CI	*p*-value
Sex	1.00	0.72 to 1.39	0.989
BW <1,500 g	3.72	2.64 to 5.27	0.001
GA <32 weeks	3.37	2.39 to 4.74	0.015
Hospital			
A			
• Total	0.38	0.23 to 0.64	<0.001
• BW <1,500 g	0.29	0.16 to 0.54	<0.001
• GA <32 weeks	0.29	0.15 to 0.54	<0.001
B			
• Total	0.92	0.65 to 1.30	0.643
• BW <1,500 g	1.11	0.69 to 1.79	0.670
• GA <32 weeks	1.10	0.66 to 1.84	0.714
C			
• Total	0.53	0.33 to 0.85	0.007
• BW <1,500 g	0.54	0.27 to 1.05	0.067
• GA <32 weeks	0.47	0.24 to 0.91	0.023
D			
• Total	0.58	0.33 to 1.04	0.067
• BW <1,500 g	0.57	0.25 to 1.26	0.161
• GA <32 weeks	0.59	0.27 to 1.27	0.173
E			
• Total	5.80	3.79 to 8.89	<0.001
• BW <1,500 g	10.12	4.59 to 22.32	<0.001
• GA <32 weeks	9.23	4.45 to 19.12	<0.001

ROP = retinopathy of prematurity; BW = birth weight; GA = gestational age; CI = confidence interval

Using the AAP 2006 ROP screening examination criteria, the average sensitivity of ROP detection were 67.6%; and to increase the sensitivity to be over 90%, infants with birth weight less than 1,935 grams or gestational age less than 34 weeks should be screened for ROP. Specific criteria for each hospital were shown in Table 5.

Table 5. Overall and individualized suggested ROP screening criteria

Hospital	AAP 2006 criteria sensitivity (%)		Suggested criteria from this study					
	BW <1,500 g	GA <32 weeks	BW criteria (g)	Sensitivity (%)	95% CI	GA criteria (weeks)	Sensitivity (%)	95% CI
A	81.0	90.5	<1,600	95.2	0.65 to 0.87	<32	90.5	0.59 to 0.83
B	71.4	80.0	<1,850	91.4	0.67 to 0.80	<34	91.4	0.63 to 0.78
C	61.5	69.2	<1,965	92.3	0.56 to 0.81	<35	92.3	0.54 to 0.78
D	62.5	75.0	<1,665	93.8	0.64 to 0.87	<36	93.8	0.49 to 0.82
E	63.6	83.1	<2,015	90.9	0.71 to 0.87	<34	93.5	0.71 to 0.87
Overall	67.6	80.5	<1,935	90.0	0.67 to 0.75	<34	91.4	0.66 to 0.74

ROP = retinopathy of prematurity; AAP = American Academy of Pediatrics; BW = birth weight; GA = gestational age; CI = confidence interval

Discussion

Compared to the previous studies, the present study showed the ROP rate in the 7th health district of Thailand at 31.7% was higher than the rate in China studied by Xu et al (17.8%)[16] and Brazil studied by Zin et al (16.7%)[7]. However, it was lower than studies conducted in Taiwan (38.7%)[15], Saudi Arabia (56.0%)[17], and Turkey (33.6%)[18]. This reflected considerable difference of ROP rate between hospitals in different countries. Expectedly, risk factors significantly associated with ROP rate according to the present study were low gestational age and low birth weight, however, survival rate had no significant association. Among hospitals within the same health district, the ROP rate differed significantly with the lowest ROP rate had been observed in hospital A which was a teaching university hospital equipped with level-3 neonatal unit while the highest ROP rate was in hospital E which was a tertiary hospital without level-3 neonatal unit. This result was consistent with the study conducted by Zin et al[7] which lower incidence of ROP was observed in higher level of neonatal unit with more available neonatologists, staffs and equipment. Interestingly, among tertiary hospitals, hospital C and D had ROP rates lower than district average while hospital E had very high ROP rate. Because the quality of neonatal care could be shown by lower neonatal complications[10,19,20], thus different ROP rates could be associated with different neonatal care practices among the hospitals included in the present study. To achieve 90% sensitivity for ROP detection, the ROP screening criteria should be adjusted to include infants with birth weight less than 1,935 grams and gestational age less than 34 weeks, but these could overwhelmingly increase the workload of the ophthalmologists. Individual ROP screening criteria for each hospital could improve the effectiveness of ROP screening with optimal increased in workload.

Conclusion

Different ROP rates were observed among the participating hospitals and assumingly caused by different neonatal care practices. Higher level of neonatal unit was associated with lower ROP rate. Individualized ROP screening criteria could improve the effectiveness of ROP detection. However, further study focusing on neonatal care practices in each hospital should be conducted to point out the root cause of ROP.

What is already known on this topic?

ROP is an important cause of blindness in premature infants. Multiple risk factors can contribute to the incidence of ROP. Different hospitals have different rate of ROP, and universal criteria for ROP screening eye examination may not be appropriated especially in area with high ROP rate such as developing countries.

What this study adds?

ROP rate at the 7th health district hospitals of Thailand was higher than in developed countries. Different hospitals indeed had different ROP rate with the lowest rate occurred at the university hospital with high-level neonatal unit. The ROP rate also differed among tertiary hospitals equipped with similar level of neonatal unit and could be caused by different neonatal care practices. Further study should be conducted. Individualized ROP screening criteria for each hospital may improve ROP detection without over increasing the workload of ophthalmologists.

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Potential conflicts of interest

The authors declare no conflict of interest.

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