

Trends in the incidence of retinopathy of prematurity over a 10-year period

Prudence P. C. Chow · Wilson W. K. Yip · Mary Ho · Julie Y. C. Lok · Henry H. W. Lau · Alvin L. Young

Received: 9 October 2017 / Accepted: 16 March 2018 / Published online: 16 June 2018
© Springer Nature B.V. 2018

Abstract

Aim To describe and evaluate the trends in the incidence of retinopathy of prematurity over a 10-year period in a tertiary hospital in Hong Kong.

Methods A retrospective review was performed on all preterm infants screened and/or treated for retinopathy of prematurity from January 2006 to December 2015 at Prince of Wales Hospital, Hong Kong. Preterm infants with incomplete records or transferred-in from other hospitals/region solely for treatment of ROP were excluded. The incidence of any ROP or Type 1 ROP was analysed with gestational age and birth weight over a 10-year period with consecutive 2-year intervals to evaluate the trends.

Results Of all 754 infants included in the study, 234 (31.0%) patients had any ROP and 34 (4.5%) infants developed Type 1 ROP. The incidence of any ROP demonstrated a statistically significant decreasing trend over the five consecutive 2-year intervals ($p = 0.016$), but the incidence trend of Type 1 ROP is not statistically significant. No infants weighing more than 1250 g developed Type 1 ROP.

Conclusion We observed a decreasing trend in the incidence of any ROP across the 10-year period in a

tertiary hospital in Hong Kong, while the incidence of Type 1 ROP remained stable at 4.5%. The factors leading to the trend were unclear. Improved prenatal care, changing proportion of cases with different birth weight and gestational age, oxygenation level practice in neonatal unit may all contribute to the decreasing trend. Revision of screening criteria may be made according to local experience to maximise cost-effectiveness.

Keywords Retinopathy of prematurity · Paediatric ophthalmology · Incidence · Trends · Hong Kong

Introduction

Retinopathy of prematurity (ROP) is one of the leading causes of preventable childhood blindness throughout the world, in particular in middle-income countries [1]. The International Classification of ROP (ICROP) standardised the terminology used to describe ROP, and a revision of the classification was published in 2005 [2, 3]. The British guidelines from the Royal College of Paediatrics and Child Health in 2008 recommended screening for ROP in premature infants with gestational age (GA) of < 32 weeks or birth weight (BW) of < 1501 g [4]. This guideline had been evaluated to be applicable to the ROP screening in Hong Kong [5]. The CRYO-ROP study, Laser ROP Study and the Early Treatment for

P. P. C. Chow · W. W. K. Yip (✉) · M. Ho · J. Y. C. Lok · H. H. W. Lau · A. L. Young
Department of Ophthalmology and Visual Sciences, 1/F Eye Centre, Prince of Wales Hospital, The Chinese University of Hong Kong, Shatin, Hong Kong
e-mail: ywk806@ha.org.hk

Retinopathy of Prematurity (ETROP) study had guided and revised the treatment modalities and indication of treatment of severe ROP [6–8].

Incidence of preterm birth (before gestational age of 37 weeks) varies across the world. In developed countries, the rate of preterm birth ranges from 5 to 13% [9]. Due to advancement of obstetric and neonatal care, the rate of preterm birth increased in many developed countries. In a retrospective cohort study in a tertiary centre in Hong Kong, the overall rate of preterm delivery was 6.5% for 1995–2011 [10]. Incidence of ROP varies greatly in different parts of the world [11, 12]. Population-based study on the incidence of ROP varies due to various reasons, e.g. difference in the proportion of preterm infants who survived, inclusion criteria for study, quality of neonatal intensive and ophthalmological care, difference in the ROP screening programme and compliance to the screening programme. In developed countries, the incidence of ROP ranges from 17 to 36.4% [13, 14].

The aim of this study is to describe and evaluate the trends in the incidence of retinopathy of prematurity over a 10-year period in a tertiary neonatal unit in Hong Kong.

Subjects and methods

This was a retrospective study conducted at Prince of Wales Hospital in Hong Kong, a tertiary hospital with neonatal intensive care unit service serving the northern part of Hong Kong. The medical records of all preterm infants screened and/or treated for retinopathy of prematurity at Prince of Wales Hospital from 1 January 2006 to 31 December 2015 were reviewed. Clinical parameters including sex, race, gestational age, birth weight, the presence of any degree of ROP in each eye, severity and type of ROP in each eye were charted. Preterm infants transferred-in from other hospitals/region solely for the treatment of ROP were excluded from this study as this was a selected treatment group transferred-in and would bias the overall trend. Infants with incomplete records were also excluded. The study protocol was approved by the Joint Chinese University of Hong Kong—New Territories East Cluster Clinical Research Ethics Committee (The Joint CUHK-NTEC CREC) under the Chinese University of Hong Kong, and is compliant

to the Declaration of Helsinki. Our hospital had been screening premature babies with < 32-week gestation or < 1501 g birth weight or those considered as high-risk cases by neonatologists were screened for ROP. The first ROP screening was performed in infants at 31-week gestational age or 4-week postnatal age, whichever was later, which was in line with the Royal College of Ophthalmologists Retinopathy of Prematurity Guideline (2008), and this guideline was formally adopted after its publication. Fundal examinations were performed by two experienced paediatric ophthalmologists. Pupils were dilated with a mixture of cyclopentolate 0.5% and phenylephrine 1.25% before fundal examination. Indirect ophthalmoscopy was performed using a 28 dioptre lens after the application of local anaesthesia and lid speculum. The stages of ROP were described according to the International Classification of Retinopathy of Prematurity (2005). Indications for treatment are Type 1 ROP and aggressive posterior ROP (AP-ROP).

The incidence of patients with any degree of ROP, Type 1 ROP in either eye was analysed with birth weight and gestational age over the 10-year period with consecutive 2-year intervals to evaluate any trends over the period. The trend analysis is performed with linear-by-linear association test in the Statistical Package for the Social Sciences (Mac version 22.0; SPSS Inc, Chicago [IL], USA).

Results

Demographics

A total of 754 infants satisfying the criteria were included in this study. Majority was of Chinese ethnicity (98.5%). The mean gestational age was 29 weeks 6 days \pm 2 weeks 3 days (range 23–37 weeks) at birth, and the mean birth weight was 1.25 ± 0.33 kg (range 0.42–2.55 kg). There were 362 girls (48.0%) and 392 (52.0%) boys. Six hundred and four cases (80.1%) had a birth weight of < 1500 g, and 623 (82.6%) of them was born before 32 weeks of gestation. Demographic details and characteristics are summarised in Table 1.

Table 1 Demographic details and patient characteristics

	2006–2007	2008–2009	2010–2011	2012–2013	2014–15
BW (kg), mean \pm SD	1.19 \pm 0.30	1.24 \pm 0.32	1.28 \pm 0.34	1.27 \pm 0.32	1.29 \pm 0.35
GA (weeks), mean \pm SD	29 ⁶ \pm 2 ³	30 \pm 2 ⁴	30 \pm 2 ³	29 ⁶ \pm 2 ²	29 ⁶ \pm 2 ²
Gender, <i>n</i> (%)					
Male	65 (51.2)	81 (52.9)	86 (54.4)	86 (50.6)	74 (50.7)
Female	62 (48.8)	72 (47.1)	72 (45.5)	84 (49.4)	72 (49.3)
Race, <i>n</i> (%)					
Chinese	126 (99.2)	151 (98.7)	153 (96.8)	168 (98.8)	145 (99.3)
Non-Chinese	1 (0.8)	2 (1.3)	5 (3.2)	2 (1.2)	1 (0.7)
BW, <i>n</i> (%)					
\leq 1000 g	39 (30.7)	38 (24.8)	38 (24.1)	42 (24.7)	34 (23.3)
1001–1250	27 (21.3)	38 (24.8)	32 (20.2)	32 (18.8)	26 (17.8)
1251–1500	47 (37.0)	55 (36.0)	52 (32.9)	54 (31.8)	50 (34.2)
$>$ 1500	14 (11.0)	22 (14.4)	36 (22.8)	42 (24.7)	36 (24.7)
GA (wks), <i>n</i> (%)					
$<$ 26	7 (5.5)	14 (9.2)	12 (7.6)	11 (6.5)	10 (6.8)
26– $<$ 28	18 (14.2)	15 (9.8)	15 (9.5)	24 (14.1)	22 (15.1)
28– $<$ 30	35 (27.6)	47 (30.7)	42 (26.6)	35 (20.6)	33 (22.6)
30– $<$ 32	46 (36.2)	41 (26.8)	58 (36.7)	82 (48.2)	56 (38.4)
\geq 32	21 (16.5)	36 (23.5)	31 (19.6)	18 (10.6)	25 (17.1)
Total number of infants	127	153	158	170	146

Incidence and trends of any ROP and Type 1 ROP

Among all the 754 infants who were included in this study, a total of 234 (31.0%) infants had some degree of ROP and 34 (4.5%) developed Type 1 ROP. To evaluate the trends in the incidence of retinopathy of prematurity over the study period, the study period was divided into five consecutive 2-year intervals: 2006–2007, 2008–2009, 2010–2011, 2012–2013 and 2014–2015. A decreasing trend in the overall incidence of any ROP was observed over this study period. The trend tested by linear-by-linear association test is statistically significant for any ROP ($p = 0.016$). The incidence of Type 1 ROP ranged from 3.4 to 5.2% over the study period intervals. The trend analysis by linear-by-linear association test is not statistically significant for Type 1 ROP. Detailed data are shown in Table 2. Among the 34 infants with Type 1 ROP, the mean GA was 26 weeks 4 days \pm 2 weeks 1 day (range 23 weeks 2 days–32 weeks) and the mean birth weight was 0.86 ± 0.19 kg (range 0.60–1.24 kg).

Subgroup analysis of any ROP and Type 1 ROP according to birth weight and gestational age

The incidence of any ROP was analysed by stratification according to birth weight and gestational age (Table 2). It remained high for the group with birth weight ≤ 1000 g (61.8–84.2%) and the group with gestation less than 28 weeks (65.6–96%). However, the trend test analysis is only statistically significant for the subgroup with gestational age between 30 and 32 weeks.

The incidence of Type 1 ROP, when analysed according to birth weight (Table 2), showed that none of the infants with birth weight above 1250 g developed Type 1 ROP over the 10-year interval and the risk of Type 1 ROP is very low for gestational age above 30 weeks. The incidence of Type 1 ROP might have a decreasing trend for the subgroup with gestational age $<$ 28 weeks although it did not reach statistically significant level.

Table 2 Incidence of any ROP and Type 1 ROP between 2006 and 2015

	2006–07	2008–2009	2010–2011	2012–2013	2014–2015	<i>p</i> value
Incidence of any ROP and Type 1 ROP						
Any ROP (%)	37.8	31.2	32.3	31.2	23.3	0.016*
Type 1 ROP (%)	4.7	5.2	5.1	4.1	3.4	0.460
Stratification of incidence of any ROP according to birth weight and gestational age						
BW (%)						
≤ 1000 g	64.1	84.2	78.9	71.2	61.8	0.513
1001–1250	44.4	31.6	37.5	43.8	23.0	0.379
1251–1500	21.3	5.5	15.4	14.8	10.0	0.474
> 1500	7.1	4.5	2.8	2.4	5.6	0.853
GA, wks (%)						
< 28	84.0	86.2	96.0	82.9	65.6	0.123
28–< 30	45.7	34.0	45.2	42.9	27.3	0.341
30–< 32	21.7	12.2	6.9	9.8	7.1	0.028*
≥ 32	5.0	5.6	12.9	5.6	0	0.519
Stratification of incidence of Type 1 ROP according to birth weight and gestational age						
BW (%)						
≤ 1000 g	12.8	18.4	13.2	7.1	11.8	0.413
1001–1250	3.7	2.6	9.4	12.5	3.8	0.395
1251–1500	0	0	0	0	0	NA
> 1500	0	0	0	0	0	NA
GA, wks (%)						
< 28	24.0	24.1	18.5	11.4	12.5	0.120
28–< 30	0	2.1	4.8	5.7	0	0.637
30–< 32	0	0	0	1.2	1.8	0.179
≥ 32	0	0	3.2	0	0	0.955
Total number of infants	127	153	158	170	146	

NA not applicable

* $p < 0.05$

Discussion

The reported incidence of ROP among developed countries varied greatly [13–19]. A recent study reported even greater variation among developed countries within selected subgroup of extremely preterm infants weighing < 1500 g at 24–27-week 6-day gestation, of which the rates of any ROP ranged from 25.2 to 91.0% [19]. Difference in survival rate of extremely preterm infants, neonatal care and practice, accuracy of diagnosis and treatment thresholds may all contribute to these variations. The reported incidence of ROP in Hong Kong varied between 16.9 and 28.2%, while Type 1 ROP remained at low incidence between 3.4 and 3.8% [5, 20, 21]. The British screening

guideline is generally adopted in Hong Kong neonatal units and was found to be applicable without missing treatment-requiring cases [5, 21]. In this study, we evaluated the trends of ROP in a tertiary centre in Hong Kong and found that the incidence of any ROP showed a general decreasing trend over our 10-year study period, while the incidence of Type 1 ROP did not show a statistically significant decreasing trend. This is consistent with the findings in a Scottish population, which observed a reduction in the incidence of any ROP from 1990 to 2004 [13]. However, a Swedish group noted that the incidence of ROP in infants with a birth weight of 1500 g or less remained the same in two consecutive populations one decade

apart [14]. Another study in Turkey noted an increased incidence of ROP over a 10-year period, but the numbers of treatment-requiring cases were similar in both periods [22]. Improved survival rates of premature infants and infants with low birth weight, however, might have resulted in an increased incidence of ROP. Higher quality of care from the neonatal intensive care might on the other hand contributed to decreased incidence of ROP. Our overall incidence of ROP is comparable with that of the developed countries [15–18], and the incidence of Type 1 ROP is 4.5% (Table 3).

It had been reported that Asian might be at a higher risk of developing threshold ROP compared to white infants [23, 24]. In our study, the percentage of any ROP for infants with weight ≤ 1000 g (61.8–84.2%) or gestational age < 28 weeks (65.6–96) was on the high side compared with those reported by Darlow et al. [19] in which any ROP rates of a selected group of preterm infants ranged from 25.2 to 91.0% in Switzerland and Japan, respectively. It is interesting that any ROP rates reported by another Hong Kong group for these subgroup infants are also similar, 70.6% for < 1000 g and 66.7% for < 28 -week gestation [21]. Whether Asian not only have higher risk of developing threshold ROP but also at risk of developing any degree of ROP will need further study.

Interestingly, an interval rise in ROP incidence around 2010–2013 was noted in our study. This period corresponded to the period when an increasing number of non-local expectant mothers had travelled from the Mainland China to Hong Kong to deliver their babies. The number of live births born in Hong Kong to

Mainland women peaked at 2010–2012. These non-local mothers frequently had no or substandard antenatal care leading to higher incidence of adverse pregnancy outcomes [25]. This might have contributed to the increase in the incidence of ROP as well as the incidence of Type 1 ROP during this period.

None of the infants with birth weight above 1250 g developed Type 1 ROP (Table 2). Only one infant who was born at 32 weeks or above had Type 1 ROP (Table 2) and that infant had extremely low birth weight of 0.65 kg. This provides supporting data for counselling parents on the prognosis and likelihood of developing severe ROP requiring treatment. It is also worthwhile to critically review the application of screening criteria to minimise unnecessary screening of very low-risk patients. For the overall decrease in ROP incidence, it is unclear and cannot be determined in this study what the contributing factors are. Improved antenatal and neonatal care may be related. Furthermore, since the incidence of Type 1 ROP is low at 4.5% in our study, a much larger sample size would be needed to demonstrate a statistically significant trend in the incidence of Type 1 ROP.

This study is the first to look at the recent trend of retinopathy of prematurity in our locality, and it has a representable sample size and covered a long period of time in a single centre. It provides useful insight into the counselling of parents and allows care providers to reflect on the cost-effectiveness of the current screening programme. This study also provides a basis for future multi-centre studies in the incidence of ROP. Limitations of this study include its retrospective

Table 3 Comparison of Hong Kong data to other countries

Country	Year	Denominator	Incidence of any ROP	Incidence of treatment-requiring ROP (%)
USA [18]	2009	Live born infants 501–1500 g	Not known	6.8
Sweden [14]	1998–2000	< 1500 g	36.4%	11.5
Scotland [13]	1990–2004	< 32 -week GA and or BW < 1500 g	17%	5
Northern Ireland [17]	2000–2011	< 32 -week GA or < 1500 g surviving to 42-week adjusted GA	Not known	3.96
Taiwan [16]	2007–2011	< 1500 g	Not known	12.3
South Korea [15]	2013–2014	< 1500 g	34.1%	11.5
Hong Kong (the present study)	2007–2015	< 32 -week GA or < 1500 g	31.0%	4.5

nature and the possible inter-observer variability between the paediatric ophthalmologists who screened all infants for ROP. There is also a lack of data on the risk factors for ROP, including multiple births, level of oxygen therapy in the neonatal unit, antenatal and perinatal events. This study was conducted in a tertiary hospital in Hong Kong, and its data cannot represent the entire population.

In conclusion, we observed a decreasing trend in the incidence of any ROP across the 10-year period from 2006 to 2015 in a tertiary hospital in Hong Kong, while the incidence of Type 1 ROP remained stable at 4.5% which is comparable to that of other developed countries. There was no case of Type 1 ROP in infants with birth weight greater than 1250 g. It is unclear what were the factors leading to the decreasing trend. Improved prenatal care, changes in survival rate of extremely preterm infants, changes in the proportion of infants with different birth weight and gestational age, practice of oxygenation level in neonatal unit and overall standard of neonatal unit, diagnosis of ROP and treatment experience may all contribute to the decreasing trend. Further analysis on the applicability of screening criteria is worthwhile. Revision of screening criteria may be made according to local condition to maximise the cost-effectiveness of screening programme.

Compliance with ethical standards

Conflict of interest The authors declared that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

References

- Gilbert C, Foster A (2001) Childhood blindness in the context of VISION 2020: the right to sight. *Bull World Health Organ* 79(3):227–232
- Garner A (1984) An international classification of retinopathy of prematurity. *Arch Ophthalmol* 102(8):1130–1134
- Gole GA, Ells AL, Katz X, Holmstrom G, Fielder AR, Capone A Jr et al (2005) The international classification of retinopathy of prematurity revisited. *JAMA Ophthalmol* 123(7):991–999
- Wilkinson AR, Haines L, Head K, Fielder AR (2008) UK retinopathy of prematurity guideline. *Early Hum Dev* 84(2):71–74
- Luk AS, Yip WW, Lok JY, Lau HH, Young AL (2016) Retinopathy of prematurity: applicability and compliance of guidelines in Hong Kong. *Br J Ophthalmol* 101(4):453–456
- Clarkson JG, Capone A, Sternberg P, Repka MX, Gilbert W, Chase C et al (1994) Laser therapy for retinopathy of prematurity [3]. *Arch Ophthalmol* 112(2):154–156
- Cryotherapy for Retinopathy of Prematurity Cooperative Group (1990) Multicenter trial of cryotherapy for retinopathy of prematurity. *Arch Ophthalmol* 108:1408–1416
- Early Treatment for Retinopathy of Prematurity Cooperative Group (2003) Revised indications for the treatment of retinopathy of prematurity: results of the Early Treatment for Retinopathy of Prematurity randomized trial. *Arch Ophthalmol* (Chicago, Ill.: 1960) 121(12):1684
- Slattery MM, Morrison JJ (2002) Preterm delivery. *Lancet* 360(9344):1489–1497
- Hui AS, Lao TT, Leung TY, Schaaf JM, Sahota DS (2014) Trends in preterm birth in singleton deliveries in a Hong Kong population. *Int J Gynecol Obstet* 127(3):248–253
- Gilbert C, Fielder A, Gordillo L, Quinn G, Semiglia R, Visintin P, Zin A (2005) Characteristics of infants with severe retinopathy of prematurity in countries with low, moderate, and high levels of development: implications for screening programs. *Pediatrics* 115(5):e518–e525
- Gilbert C (2008) Retinopathy of prematurity: a global perspective of the epidemics, population of babies at risk and implications for control. *Early Hum Dev* 84(2):77–82
- Dhaliwal C, Fleck B, Wright E, Graham C, McIntosh N (2008) Incidence of retinopathy of prematurity in Lothian, Scotland, from 1990 to 2004. *Arch Dis Child Fetal Neonatal Ed* 93(6):F422–F426
- Larsson E, Carle-Petelius B, Cernerud G, Ots L, Wallin A, Holmström G (2002) Incidence of ROP in two consecutive Swedish population based studies. *Br J Ophthalmol* 86(10):1122–1126
- Hwang JH, Lee EH, Kim EAR (2015) Retinopathy of prematurity among very-low-birth-weight infants in Korea: incidence, treatment, and risk factors. *J Korean Med Sci* 30(Suppl 1):S88–S94
- Su YY, Wang SH, Chou HC, Chen CY, Hsieh WS, Tsao PN et al (2016) Morbidity and mortality of very low birth weight infants in Taiwan—changes in 15 years: a population based study. *J Formos Med Assoc* 115(12):1039–1045
- Chamney S, McGrory L, McCall E, Twaij S, Napier M, Rollins R et al (2015) Treatment of retinopathy of prematurity in Northern Ireland, 2000–2011: a population-based study. *J Am Assoc Pediatr Ophthalmol Strabismus* 19(3):223–227
- Horbar JD, Carpenter JH, Badger GJ, Kenny MJ, Soll RF, Morrow KA, Buzas JS (2012) Mortality and neonatal morbidity among infants 501 to 1500 grams from 2000 to 2009. *Pediatrics* 129(6):1019–1026
- Darlow BA, Lui K, Kusuda S et al. (2017). International variations and trends in the treatment for retinopathy of

- prematurity. *Br J Ophthalmol*. <https://doi.org/10.1136/bjophthalmol-2016-310041>
20. Yau GS, Lee JW, Tam VT, Liu CC, Yip S, Cheng E et al (2016) Incidence and risk factors of retinopathy of prematurity from 2 neonatal intensive care units in a Hong Kong Chinese population. *Asia Pac J Ophthalmol* 5(3):185–191
 21. Iu LP, Lai CH, Fan MC, Wong IY, Lai JS (2017) Screening for retinopathy of prematurity and treatment outcome in a tertiary hospital in Hong Kong. *Hong Kong Med J* 23(1):41–47
 22. Demir S, Yücel ÖE, Niyaz L, Karakuş G, Arıtürk N (2015) Incidence of retinopathy of prematurity in the middle Black Sea region of Turkey over a 10-year period. *J Am Assoc Pediatr Ophthalmol Strabismus* 19(1):12–15
 23. Aralikatti AK, Mitra A, Denniston AK, Haque MS, Ewer AK, Butler L (2010) Is ethnicity a risk factor for severe retinopathy of prematurity? *Arch Dis Child Fetal Neonatal* Edit 95(3):F174–F176
 24. Husain SM, Sinha AK, Bunce C, Arora P, Lopez W, Mun K et al (2013) Relationships between maternal ethnicity, gestational age, birth weight, weight gain, and severe retinopathy of prematurity. *J Pediatr* 163(1):67–72
 25. Yung WK, Hui W, Chan YT, Lo TK, Tai SM, Sing C et al (2014) Social obstetrics: non-local expectant mothers admitted through accident and emergency department in a public hospital in Hong Kong. *Hong Kong Med J* 20(3):213–221