·Clinical Research·

Prevalence of retinopathy of prematurity in Brunei Darussalam

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Abstract

• AIM: To identify the prevalence of retinopathy of prematurity (ROP) among preterm neonates admitted to Department of Neonatology, RIPAS hospital, Brunei Darussalam.

• METHODS: We studied 67 preterm infants fulfilling the eligibility criteria for ROP screening. All infants studied were admitted to the Department of Neonatology, RIPAS Hospital, within a period of one year. Birth weight (BW), gestational age (GA), corrected age at each review, initial and final diagnoses and number of reviews required was recorded for each infant. Infants were followed up two weekly until they reach a corrected age of 40 weeks or complete vascularization was noted. Prevalence of ROP was identified. Descriptive analysis, regression analysis and independent-sample *t*-test were used to statistically check for differences between ROP and non -ROP groups.

• RESULTS: A total number of 201 ROP screenings were carried out for 67 preterm infants. Males outnumbered females (56.7%). The mean number of reviews per child was (3.19±1.1) times (range: 1-6 times), the mean GA among the preterm babies examined was (29.5 ±2.6) weeks (range: 23 -36 weeks), and the mean BW was 1300±500g (range: 660-3600g). The prevalence of ROP among the examined infants was 34.8%. Prevalence of threshold disease that required laser treatment was 25.4%. Prevalence of ROP among those with extremely low BW was 86.7% compared to 27.8% in those with very low BW. Respiratory distress and congenital heart diseases were significantly associated with higher incidence of ROP.

• CONCLUSION: Lower BW, lower GA and female gender are associated with higher risk of developing ROP among preterm infants in Brunei Darussalam.

• **KEYWORDS:** retinopathy of prematurity; preterm; very low birth weight; extremely low birth weight
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INTRODUCTION

Retinopathy of prematurity (ROP) is a proliferative disease affecting preterm infants. It is characterized by lack of blood vessels to the peripheral retina resulting in neovascularization which, if not treated, may progress to retinal detachment and irreversible blindness. The disease was first described in 1940s, as 'Retrolental Fibroplasia' [1]. ROP is an important cause of avoidable blindness among children. It accounts for up to 10% of childhood blindness in developed countries[2]. Gestational age (GA) and birth weight (BW) are the main factors affecting the prevalence and severity of ROP[3].

The prevalence of ROP appears to be higher in South East Asia compared to rest of the world. In Brazil, the prevalence of ROP was 48.9% among infants with extremely low BW (ELBW), and 18.2% in infants with very low BW (VLBW)[4]. Similar studies done in this region reported a prevalence of ROP in ELBW infants of 58.6% in Malaysia [5], while the prevalence among infants with VLBW was found to be (29.2%) in Singapore[2].

There is no previous data published from Brunei Darussalam on ROP. The main aim of this paper is to establish the prevalence of ROP among the different BW groups of premature babies. This article adds on to the evidence of a higher prevalence of ROP in this region.

SUBJECTS AND METHODS

Subjects This retrospective, cross-sectional, study included all preterm infants admitted to the Neonatology department, RIPAS hospital, Bandar Seri Begawan, Brunei Darussalam, in the period from January 1, 2011 to December 31, 2011 and fulfilled the eye department's eligibility criteria for ROP screening (GA of 32 weeks or less, and/or birth weight 1 500g or less, or preterm baby of any GA with history of intrauterine growth retardation, respiratory distress syndrome and exposure to high concentrations of oxygen and positive ventilation). For the purpose of this study, threshold disease

was defined as ROP that fulfils the criteria of Early Treatment ROP Study (ET-ROP) type 1 ROP classification "zone I, any stage ROP with plus disease (a degree of dilation and tortuosity of the posterior retinal blood vessels meeting or exceeding that of a standard photograph); zone I, stage 3 ROP without plus disease; or zone II, stage 2 or 3 ROP with plus disease). ROP stage 3 zone 3, or any stage with plus disease (tortuous and dilated retinal vessels with/without difficulty in pupil dilatation)" [6].

Methods Infants included in the study were examined for ROP screening every two weeks until a corrected age of 40 weeks; or on discharge from the Neonatology department. The first examination was performed after 4 weeks of delivery or at the age of 32 weeks, whichever was earlier. Infants diagnosed with threshold disease received indirect retinal laser treatment under general anaesthesia. Those diagnosed with sub-threshold disease were examined weekly until either regression was seen or they reached threshold disease.

A data sheet including date of birth, gender, GA, BW, corrected age and diagnosis at each review was filled for all infants included in the study. Based on the birth BW, ELBW was defined as BW of 1 000g or less; VLBW was defined as BW more than 1 000g but not more than 1 500g; LBW group was defined as BW more than 1 500g but less than 2 500g.

Statistical Analysis Data analysis was done using SPSS version 15.0. Descriptive analysis was done to study the sample biometrics. Independent sample t-test was done to compare the variables in ROP (23 infants) and non-ROP (44 infants) groups. Bivariate Correlation analysis was used to study the relationships between different variables included in this study. $P<0.05$ was considered significant.

RESULTS

In year 2011, a total of 525 neonates were admitted to the Neonatology department in RIPAS hospital, of those 67 were screened for ROP; 38(56.7%) were males. The mean number of reviews per child was (3.19±1.1) times (range: 1 time-6 times), the mean GA among the preterm babies examined was (29.5±2.6) weeks (range: 23-36 weeks), and the mean BW was (1321±500)g (range: 660-3600g). BW was 1 500g or less in 72.2% of the infants. GA was 28 weeks or less in 35.8% of the infants studied.

Out of 67 infants examined, 23 (34.8%) had some degree of ROP and 17 (25.4%) had, or developed at a later review, a threshold ROP that required laser treatment. After laser treatment, ROP regressed in all infants except in one (BW=660g, GA=26 weeks) who progressed to stage 4 (Table 1).

The presence and stage of ROP was significantly related to lower BW and GA (Table 2). Lower GA was also found to be significantly related with worse initial diagnosis and worse final diagnosis, indicating less response to laser treatment ($P<0.001$, $P=0.005$ respectively). Similarly, a lower BW was significantly related to worse initial diagnosis, but did not significantly correlated to worse final outcome ($P<0.001$ and $P=0.056$ respectively).

Infants with ELBW had a much higher prevalence of ROP (86.7%) compared to VLBW group (27.8%). Infants with BW more than 1 500g did not have ROP among this study group. ELBW group was also associated with a need for more laser treatments compared to the VLBW group (Table 3). Of all infants diagnosed with ROP, 73.9% needed laser treatment, while the rest regressed spontaneously.

Independent sample t-test was done to compare the different variables studied in the ROP and the non-ROP groups. Among the two groups, females were significantly more in the ROP group "64.7%" compared to the non-ROP group

Table 1 Characteristics of the ROP patients who received laser treatment

Case (*n*)	GA (weeks)	BW (g)	CA at first visit (weeks)	Pre-laser ROP (Stage/Zone)	Final outcome (Stage/Zone)
1	28	980	32	3/2	Regressed
2	28	910	32	3/2	Regressed
3	29	1015	33	3/3	2/3
4	29	1190	33	3/2	Regressed
5	23	820	31	3/2	Regressed
6	23	750	32	3/2+	2/2
7	29	1220	34	3/3+	2/3
8	28	1150	32	3/2	Regressed
9	26	880	30	3/3+	Regressed
10	26	755	30	3/2	Regressed
11	30	1180	34	3/3+	Regressed
12	27	800	31	3/3	Regressed
13	27	840	31	3/3	Regressed
14	25	660	31	3/2+	4/2
15	26	920	31	3/3	Regressed
16	30	1210	34	3/3+	Regreesed
17	30	1150	34	3/3+	Regressed

GA: Gestational age; BW: Birth weight; CA: Corrected age; ROP: Retinopathy of prematurity.

Table 2 The main characteristics of the ROP group compared to the non-ROP group and the total sample of the study $\bar{x} \pm s$

Characteristics	ROP group	Non-ROP group	Total preterms examined
BW (g)	974±192	1491±525	1321±500
GA (weeks)	27.43±2.04	30.51±2.33	29.45±2.64
CA at first review (weeks)	33.00±2.54	35.15±1.83	34.29±2.39
Number of reviews	3.83±1.03	2.77±0.96	3.19±1.10

BW: Birth weight; GA: Gestational age; CA: Corrected age; ROP: Retinopathy of prematurity.

Table 3 Distribution of study sample, presence of ROP and number of cases that required laser treatment among the three birth weight groups *n*(%)

Paramenters	ELBW	VLBW	LBW	Total
Infants	15(22.4)	36(53.7)	16(23.9)	67(100)
ROP present	[1]13(86.7)	[1]10(27.8)	[1]0(0)	[1]23(34.3)
Laser done	[1]11(84.6)	[1]6(60)	[1]0(0)	[1]17(73.9)

[1]Percentage is counted from the number in the cell above within the same column. ELBW: Extremely low birth weight (BW ≤1 000g); VLBW: Very low birth weight (BW >1 000g but ≤1 500g); LBW: Low birth weight (BW >1 500g but <2 500g); ROP: Retinopathy of prematurity.

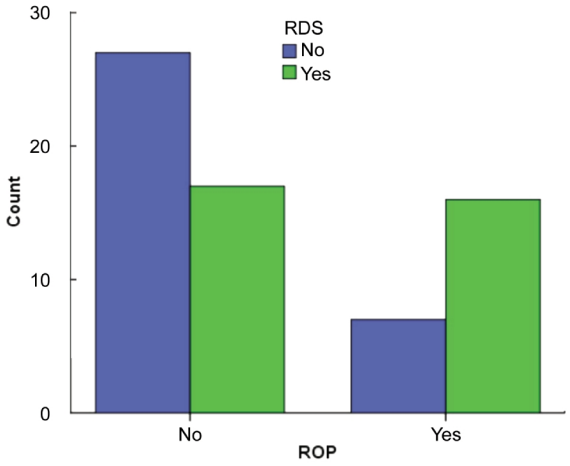

Figure 1 Bar chart showing the presence of Respiratory distress syndrome (RDS) among the ROP and the non-ROP groups.

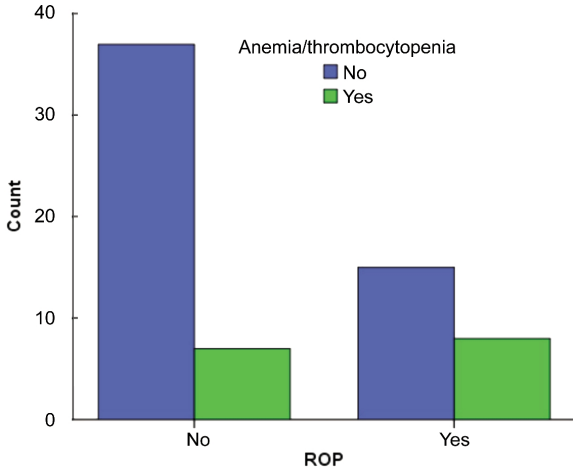

Figure 2 Bar chart showing the presence of anemia and/or thrombocytopenia among the ROP and the non-ROP groups.

"31.4%" (P=0.028 "95% CI:-0.610-0.037"). BW and GA were both significantly lower in the ROP group compared to the non-ROP group (P<0.001 "95% CI:1.922-4.232" and P< 0.001 "95% CI:-0.610-0.037" respectively).

Systemic risk factors such as respiratory distress syndrome (RDS), anemia and/or thrombocytopenia, congenital heart diseases (CHD) and septicemia were also studied among the ROP and the non-ROP groups. Figures 1, 2, 3 and 4 show the frequency of these conditions among the two groups. Pearson's Chi-square test showed that RDS and CHD were associated with significantly higher incidence of ROP (P= 0.016 and P=0.028 respectively). The presence of anemia and septicemia, on the other hand, showed no significant relationship with the presence of ROP (P=0.078 and P= 0.149 respectively).

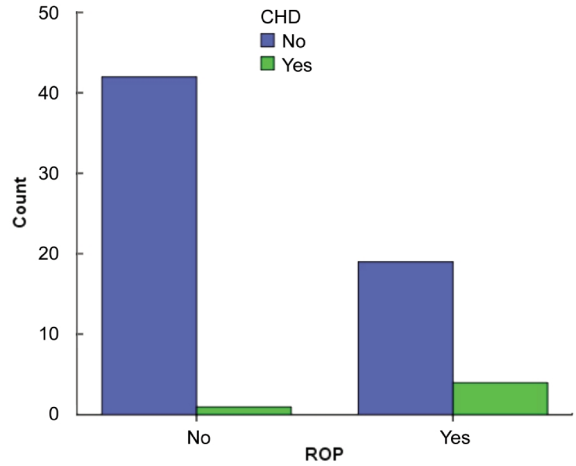

Figure 3 Bar chart showing the presence of congenital heart diseases (CHD) among the ROP and the non-ROP groups.

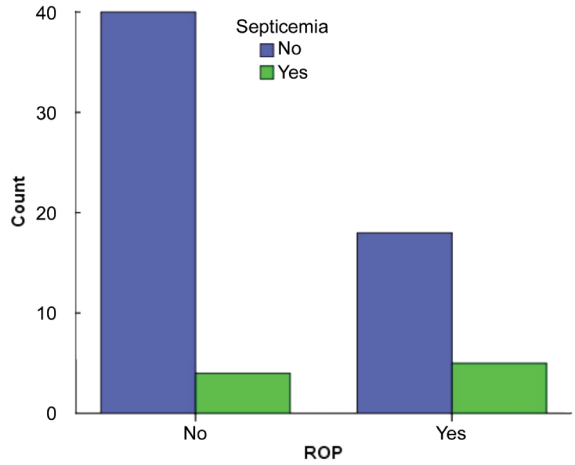

Figure 4 Bar chart showing the presence of septicemia among the ROP and the non-ROP groups.

DISCUSSION

During embryonic life, retinal vascularization starts in the 16th week of gestation. Blood vessels grow out of the optic disc into four bundles of spindle cells forming the four main vascular arcades of the central retinal artery. Vascularization of the nasal retina up to the ora serrata is completed by 32 weeks of gestation. Blood vessels reach the temporal ora serrata by the age of 36-40 weeks of gestation. Premature delivery may disrupt this process forming an avascular peripheral zone which may develop subsequent ischaemia and proliferative reaction. When threshold disease is diagnosed, the peripheral avascular retina should be ablated (either by laser or cryotherapy) to stop the neovascularization process and prevent irreversible blindness.

In 1980s, the Cryotherapy ROP Study (Cryo-ROP) found that applying cryotherapy to the avascular zone of the retina halted the risk of vision loss in infant with threshold ROP disease defined by the study that time [7]. In 2002, ET-ROP study found that high risk pre-threshold ROP benefited also benefited from being treated. Thus, threshold disease was pushed one step ahead[6]. This study adopted the level of ROP recommended by ET-ROP study for laser treatment as the threshold disease.

Brunei Darussalam has an area of 5 765km^2, with an estimated population of 415 717[8]. RIPAS hospital is the only tertiary centre in the country. The sample size of this study reflects and represents, proportionately, the neonatal population of the country.

The prevalence of ROP among the sample of this study was 34.8%. Infants with ELBW, BW<1 000g, had higher prevalence of ROP (86.7%) compared to VLBW, BW ≤1 500g but >1 000g, infants (27.8%). The results among VLBW infants were comparable to previous studies from the neighbouring regions. However, in our study, a higher prevalence is apparent among ELBW infants compared to studies from nearby regions. In 1994, Leo and Cheong [9] reported ROP in 34.4% in infants weighing less than 1 250g in Singapore. Shah *et al* [2], similarly, reported a prevalence of 29.2% among VLBW infants in Singapore. On the other hand, Choo *et al* [5] from Malaysia, reported a prevalence of ROP of 58.6% among ELBW infants in a sample of 70 eligible infants. Another study from Bangladesh reported ROP prevalence of 4.4% among neonates in their setup [10]. This low prevalence of ROP can be attributed to the higher neonatal mortality rate among preterm babies (769/1 000 in preterm neonates <32 weeks of gestation) [11]. The high prevalence of ROP in our centre reflects the highly advanced health resources available in Brunei, resulting in an increasingly growing survival rate among extremely preterm neonates (as young as 23 weeks of gestation), of extremely low BW (as low as 660g).

In their study, Araz-Ersan *et al* [12] reported significant association between the presence of ROP and male gender, RDS and sepsis. We found a similar relation between RDS and ROP. However, our results showed female preponderance among the ROP group, and we found no significant relationship between ROP and sepsis.

Likewise, Zhu *et al* [13] reported significantly higher incidence of ROP among preterms with anemia, which we failed to prove in our study.

Our study supported the findings of Johns *et al* [14] with regards to the significant association between the presence of ROP and CHD.

The prevalence and the severity of ROP is expected to further increase with the ever growing numbers of extremely premature neonates surviving in neonatology departments worldwide. Patients with RDS and CHD are at higher risk of developing ROP, thus careful ROP screening should be performed routinely in this group of preterm babies.

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