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Characteristic and risk factors of retinopathy of prematurity in Sanglah Hospital Denpasar: 3-years retrospective study

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ABSTRACT

Introduction: Retinopathy of prematurity (ROP) is one of the important causes of blindness in children. ROP is characterized by abnormal retinal neovascularization of premature infants.

Purpose: This study aimed to estimate the prevalence of ROP in preterm infants at Sanglah Hospital Bali from 2015-2017 and identify the risk factors predisposing them to ROP.

Methods: This was a retrospective study, observational analysis on premature infants diagnosed as ROP at Sanglah Hospital Bali from January 2015 to December 2017, with a gestational age of 30 weeks or less at birth and a birth weight of 1500 grams or less. Infants whose gestational age was >30 weeks or whose birth weight was >1500 grams were also included. The ophthalmological examinations were initiated between the fourth and sixth weeks of chronological age or 34 weeks of corrected age, whichever was earlier, and were repeated weekly or biweekly as per Indonesian guidelines for ROP screening, until full vascularization of the retina reached zone 3.

Results: Out of 31 infants diagnosed as ROP, 3 (9.7%) cases developed ROP in one eye, and 28 (90,3%) cases in both eyes. They were classified as 23 (74.2%) cases stage 1, and 8 (25,8%) cases stage 2. None of the studied infants presented ROP at stage 3, 4, or 5. The risk for ROP was not significantly associated with birth weight (OR 0.375; 95% CI 0.030 – 4.635), gestational age (OR 0.897; 95% CI 0.792 – 1.015), sepsis (OR 1.111; 95% CI 0.089 – 13.835), blood transfusion (OR 1.111; 95% CI 0.089 – 13.835), and HMD (OR 1.118; 95% CI 0.977 – 1.443).

Conclusions: The data of this study showed that low gestational age, low birth weight, sepsis, oxygen therapy, and blood transfusion may be contribute to the development of ROP, but not significant statistically. Clinicians should be aware of the presence of the additional risk factors when monitoring preterm infants,especially when giving supplemental oxygen therapy.

Keywords: characteristics, infants, retinopathy of prematurity, risk factors.
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INTRODUCTION

Retinopathy of prematurity (ROP) is one of the important causes of blindness in children. ROP is characterized by abnormal retinal neovascularization of premature infants. Retinal detachment is the main cause of visual impairment and blindness in ROP.[1,2] Many studies suggest that blindness due to ROP varies enormously, and more than 50.000 children are blind due to ROP.[3] In Indonesia, the incidence of ROP in 2017 was around 18-30% and blindness was found in up to 35 weeks infants.[4]

The rapid development in neonatal care has improved the survival rates for premature infants. This progress increases the incidence of ROP in parallel. Many studies report the increasing survival rates of preterm infants due to improved quality of perinatal care.[5,6] The pathogenesis of ROP is divided into two phases. In phase I, there is insufficient vascularization of the developing retina creates hypoxia, which precipitates the release of factors stimulating abnormal blood vessel growth, called phase II.[7]

Retinopathy of prematurity classification was formed in 1984 by dividing the retina into three zones, extending from the posterior to the anterior retina and describing the extent of ROP in clock hours of involvement. The severity of ROP is categorized into 5 stages: stage 1 is a flat demarcation line of abnormal fibrovascular tissue at the junction of the vascular and avascular retina; stage 2 is a ridge of fibrovascular tissue; stage 3 represents the increasing volume of retinal and extraretinal neovascularization; stage 4 indicates partial retinal detachment; and stage 5 is total retinal detachment. Increased dilation and tortuosity of posterior retinal vessels is described as «plus disease» an ominous sign of active and progressive disease.[8]

The treatment recommendations are based on the Early Treatment For Retinopathy of Prematurity (ETROP) Study. This study divided ROP into 2

groups, type 1 and type 2 ROP. Type 1 ROP includes in zone 1, any ROP with plus disease or stage 3 ROP without plus disease, and in zone 2, stage 2 or 3 ROP with plus disease, which the treatment should be considered. For type 2, eyes only be observed and treated if type 1 ROP develops.[9]

The pathogenesis of ROP is associated with excessive oxygen use. However, many study reports have found other factors influencing ROP development, such as low gestational age, low birth weight, supplementary oxygen, sepsis and frequent blood transfusions. The roles of these factors are still as controversial.[10–13] This study aimed to estimate the prevalence of ROP in preterm infants at Sanglah Hospital Bali from 2015-2017 and identify the risk factors predisposing to ROP.

MATERIALS AND METHODS

This study was a retrospective, observational analysis of premature infants diagnosed as ROP at Sanglah Hospital Bali from January 2015 to December 2017, with a gestational age of 30 weeks or less and a birth weight of 1500 grams or less. Infants whose gestational age was >30 weeks or whose birth weight was >1500 grams were also included. Infants who died before the first ophthalmologic examination were excluded.

All examinations were performed at Sanglah Hospital Bali between 2015-2017. The infants were examined while hospitalized and as outpatients. The examination consisted of binocular indirect ophthalmoscopy with a 20-diopter lens and a lid speculum. Pupils were dilated with 0,5 % tropicamide, and 2,5 % phenylephrine eye drops, applied one hour before the examination. Scleral indentation was done only if necessary, to view the peripheral retina. All exams were performed by a single ophthalmologist qualified to conduct ROP screening. The ophthalmological examinations were initiated between the fourth and sixth weeks of chronological age or 34 weeks of corrected age, whichever was earlier, and were repeated weekly or biweekly as per Indonesian guidelines for ROP screening until full vascularization of the retina reached zone 3.

After recording the data, the presence of retinopathy was graded by location (zone 1-3), severity (stage 1-5), according to the criteria of The International Classification of Retinopathy of Prematurity (ICROP), and ETROP classification (type 1 and 2). Subjects› demographic data included gestational age (GA), birth weight (BW), and gender. Clinical data included laterality, supplemental oxygen treatment, sepsis, hyaline membrane disease (HMD) and blood transfusion. Our study was carried out after approval by the hospital›s ethical committee. Informed consent were obtained from the parents of the subjects.

Data were analyzed by the Statistical Package for the Social Sciences (SPSS for windows, version 23.0). Descriptive statistics as percentage for categorical variables. The Fisher›s exact test did group comparisons for categorical variables. A logistic regression model was performed and the adjusted OR (95% CI) was obtained for the risk factors. A probability (p) < 0.05 was considered significant.

RESULTS

The study population included 31 preterm infants from January 2015 to December 2017. Out of the 31 infants, 14 (45,2%) were males, and 17 (54,8%) were females. There were 17(54,8%) infants with gestational age ≤ 30 weeks, and 14 (45,2%) infants with gestational age <30 weeks. Infants with birth weight ≤1500 grams were 29 (93,5%) of cases, and >1500 gram were 2 (6,5%) of cases (Table 1).

Out of 31 infants diagnosed as ROP, 3 (9.7%) cases developed ROP in one eye, and 28 (90,3%) cases in both eyes. They have classified as 23 (74.2%) cases in stage 1 and 8 (25,8%) cases in stage 2. None of the studied infants presented ROP at stages 3, 4, or 5 (Table 2).

Table 3 showed the risk for ROP was not significantly associated with birth weight (OR 0.375; 95% CI 0.030 – 4.635), gestational age (OR 0.897; 95% CI 0.792 – 1.015), sepsis (OR 1.111; 95% CI 0.089 –

Table 1. Demographic Data of Research Respondent.

Data		Frequency (%)
Gender	Male	14 (45,2)
	Female	17 (54,8)
GA	≤30 weeks	17 (54,8)
	>30 weeks	14 (45,2)
BW	≤1500 gram	29 (93,5)
	>1500 gram	2 (6,5)

Table 2. Clinical Data of Research Respondent.

Data		Frequency (%)
Stage ROP	Stage 1	23 (74,2)
	Stage 2	8 (25,8)
	Stage 3	0
Zone ROP	Zone 1	8 (25,8)
	Zone 2	22 (71,0)
	Zone 3	1 (3,2)
	Zone 4	0
	Zone 5	0
Laterality	Unilateral	3 (9,7)
	Bilateral	28 (90,3)
Type ROP	Type 1	3 (9,7)
	Type 2	28 (90,3)
O_2 therapy	Yes	31 (100)
	No	0
Sepsis	Yes	20 (64,5)
	No	11 (35,5)
Blood transfusion	Yes	20 (64,5)
	No	11 (35,5)
HMD	Yes	12 (38,7)
	No	19 (61,3)

Table 3. Relationship of Risk Factors and Type of ROP.

Data		Type 1	Type 2	OR	95% CI	p-value
GA	≤ 30 weeks	3 (10,3 %)	26 (89,7%)	0.897	0.792 – 1.015	0.425
	> 30 weeks	0 (0)	2 (100%)			
BW	≤ 1500 gram	1 (5,9 %)	16 (94,1 %)	0.375	0.030 – 4.635	0.813
	> 1500 gram	2 (14,3 %)	12 (85,7 %)			
Sepsis	Yes	2 (10,0 %)	18 (90,0 %)	1.111	0.089 – 13.835	0.719
	No	1 (9,1 %)	10 (90,9 %)			
Blood transfusion	Yes	2 (10,0 %)	18 (90,0 %)	1.111	0.089 – 13.835	0.719
	No	1 (9,1 %)	10 (90,9 %)			
HMD	Yes	0 (0)	12 (100 %)	1.118	0.977 – 1.443	0.216
	No	3 (15,8 %)	16 (84,2 %)			

13.835), blood transfusion (OR 1.111; 95% CI 0.089 – 13.835), and HMD (OR 1.118; 95% CI 0.977 – 1.443).

DISCUSSION

Retinopathy of prematurity is a major cause of preventable blindness in children worldwide. The American Academy of Ophthalmology has published a guideline for ROP screening, which is that infants weighing less than 1500 grams or gestational age ≤30 weeks and infants weighing between 1500 and 2000 grams or gestational age >30 weeks with an unstable clinical course should receive dilated ophthalmoscopy examinations for ROP.[14]

Demographic factors may influence the development of ROP. This study found nearly equal numbers of male and female infants. This result is similar to another report.[9,15] However, another study showed that male infants have a significantly higher incidence of ROP than females.[16] The reason for the better outcomes for female infants is still unclear, but it has been suggested due to a different hormonal condition associated with organ maturation.[17]

Many studies report that low gestational age is associated with lower birth weight on ROP development. Most of the worldwide data of ROP includes patients with birth weight <1500 grams and/or gestational age <32 weeks. Lower gestational age is associated with a shorter duration of maternal protection and longer exposure to an extrauterine environment. These factors may play a big role in the development of ROP itself.[9,15–20] In our study, we found a higher number of cases of ROP in infants with lower gestational age and lower birth weight, although it was insignificant statistically.

Our data showed that all ROP infants received supplemental oxygen therapy. From this result, it is possible to suggest that the prevalence in the exposed infants is greater compared to the non-exposed ones. Oxygen therapy is associated with hyaline membrane disease, which occurs almost exclusively in premature infants.[2,7,11,15,16] But in our study, hyaline membrane disease was not significantly associated with ROP.

This study found that sepsis was not significantly associated with developing ROP. Our study result is the same as the studies by Chaudhari et al. dan Smith.[21,22] However, another study conducted by Shah et al. and Vinekar et al. found different results.[23,24] The relationship of sepsis and ROP is explained by the effect of endotoxins on retinal blood vessels.

The relationship of blood transfusion and ROP is still controversial. We found that the frequency of blood transfusion was not a significant risk factor for ROP. This disagreed with another study, stating that red blood cells are rich in 2,3 DPG and hemoglobin binds less firmly to oxygen, thus releasing excess oxygen to the retinal tissue. This process causes hyperoxia, free radical release, and reflex vasoconstriction leading on to ROP.[2] However, another study showed that iron excess may be associated with the development of ROP, as a free radical risk factor.[25]

The limitations of this study are the small number of patients and incomplete data about another systemic condition and frequency of oxygen therapy. Clinicians should be aware of the presence of the additional risk factors when monitoring preterm infants, especially when giving supplemental oxygen therapy. All efforts must be made to prevent blindness due to ROP.

CONCLUSION

In conclusion, the data of this study showed that low gestational age, low birth weight, sepsis, oxygen therapy, and blood transfusion may be contributed to the development of ROP, but not significant statistically.

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Declared none.

STATEMENT OF ETHICS

Ethical approval has been given by Ethical Commission of Udayana University/ Sanglah General Hospital. All human research procedures followed were in accordance with ethical standards of the committee responsible for human experimentation (institutional and national), and with the Helsinki Declaration of 1975, as revised in 2013.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest, financial or otherwise.

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AUTHOR CONTRIBUTIONS

All of the authors name list were contributed as a substantial contributor.

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