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A cross sectional study on prevalence and risk factors of retinopathy of prematurity in a tertiary care centre in Chidambaram, Tamil Nadu

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Abstract
Background: The incidence of ROP in India was reported to be 38 to 47%. The emergence of ROP was the end result of complex interaction between multiple factors.
Objectives: To find out the incidence of retinopathy of prematurity. To identify the risk factors which predispose to the development and progression of retinopathy of prematurity.
Methodology: The present study was hospital based descriptive study carried out in the department of ophthalmology, Rajah Muthiah Medical College and Hospital, Annamalai University, Chidambaram between January 2020 to March 2021. The study was carried out among infants born during the study period. They were screened for the emergence of ROP. All the sociodemographic and maternal related variables have been recorded on a proforma. The master chart was then created and analysed using SPSS version 26.
Results: Out of the 86 study participants, 53.5% were male, 50% belonged to gestational age of > 32 weeks, 73.3% were weighted less than or equal to 1500 grams and 26.7% were >1500 grams, 57% participants' mothers had normal delivery, 83.7% of the mother had singleton delivery and 76.7% required oxygen supplementation. Among infants with birth weight less than or equal to 1500 grams, 23.8% had ROP, infants whose mother had gestational age <30 weeks, 33.3% infants who received oxygen supplementation had ROP. Among the study infants who had sepsis 58.3% had ROP. In the present study participants who received exchange transfusion 59.3% had developed ROP, variables like phototherapy, mode of delivery and twin delivery were not statistically significant.
Conclusion: The prevalence of retinopathy of prematurity was found to be on the higher side in the study population. Lower birth weight, lower gestational age, presence of RDS, history of sepsis and exchange transfusions were found to be the risk factors associated with ROP.

Keywords: ROP, sepsis, birth weight, gestational age, exchange transfusions, RDS

Introduction
In the late 1940s, retinopathy of prematurity appeared suddenly in preterm infants. The disorder, initially called retrolental fibroplasia, was characterised by a complete retinal detachment behind the lens. The cause of this first wave of retinopathy of prematurity was the use of supplemental oxygen in closed incubators, which helped to improve the survival of preterm infants, but also contributed to blindness [1].
The key pathological change is local ischemia with subsequent peripheral retinal neovascularization. This may regress completely or leave sequelae from mild myopia to bilateral total blindness. It is recognized by the World Health Organization within its VISION 2020: Right to Sight program initiative as an important, potentially avoidable cause of blindness in children. The proportion of blindness as a result of ROP varies greatly among countries depending on their level of development, being influenced by the availability of neonatal care, neonatal outcome, and whether effective screening and treatment programs are in place [2].
Retinopathy of prematurity (ROP) became the major cause of blindness in children in Europe and North America during the late 1940's and 1950's after the introduction of intensive neonatal care with unmonitored supplemental oxygen for preterm and low-birth weight babies (the "first epidemic"). Since then, increased awareness of the importance of monitoring blood gases has resulted in a lower incidence of potentially blinding ROP, except in extremely low-birth weight babies, less than 1000gms at birth-i.e. in whom the "second epidemic" occurred. Data from industrialized countries suggest that up to 8% of extremely low-birth weight infants become blind from ROP [3, 4].

In India, with the development of neonatal intensive care units, premature infants with extremely low birth weights are surviving and are at highest risk of developing ROP [5]. Although it has been more than 3 decades since the establishment of safety and effective prophylaxis against ROP-blindness using laser photocoagulation or cryotherapy, there is still a lack of uniform agreement and implementation of updated NICU-based effective and timely ROP screening program in many neonatal centres in India. Indian studies have reported the incidence of ROP in premature infants as 38-47%.

The emergence of retinopathy of prematurity depends on the interaction of multiple factors, such as: gestational age, low birth weight, hypoxia, duration of oxygen supplementation, respiratory distress syndrome, twin pregnancy, anaemia, blood transfusions, sepsis, intraventricular haemorrhage, hypotension, hypothermia, etc. Till date there have been very few studies on the incidence of ROP in the state of Tamil Nadu. Hence, a study was planned to explore the incidence and to identify the risk factors of retinopathy of prematurity in NICU of a tertiary care center.

Materials and Methods

A ROP prospective screening survey was conducted by enrolling all premature admitted in Rajah Muthiah Medical College and Hospital, with a gestational age of 34 weeks or less at birth and a birth weight of 2000 g or less between January 2020 and March 2021. Infants whose gestational age was more than 34 weeks or birth weight was more than 2000 g are included if they were exposed to oxygen therapy or other risk factors. Ethical clearance for the study was obtained from the institutes ethical committee. Infants with congenital anomalies, chromosomal abnormalities, inborn errors of metabolism are excluded from the study.

A pretested semi structured proforma was used for collecting the data. History of sepsis (foul smelling liquor, premature rupture of membrane more than 18 hours, maternal urinary tract infection, and intrapartum fever more than 38 °C), and perinatal asphyxia were recorded. Present history of respiratory distress requiring therapy oxygen, sepsis, phototherapy, congenital heart disease, and blood transfusion were recorded. Prematures screened by indirect ophthalmoscopy from the fourth postnatal week and followed up periodically. Perinatal risk factors for ROP are to be assessed using univariate and multivariate analysis. Also, infants who are born between 32- and 34-weeks gestational age were examined if they had a course of instability (like sepsis, asphyxia or ventilation).

Statistical analysis

All the data collected were entered into Microsoft excel 2019 in order to create the master chart. The master chart was then loaded on to SPSS version 26 for further analysis. Both quantitative and qualitative variables were present in the study. Quantitative variables were converted to qualitative variables for further analysis. In order to describe the variables, proportion/ percentages were used and in order to find out the association between risk factor and the occurrence of ROP, chi square test was applied.

Results

Table 1: Baseline characteristics among the study participants

Variable		Frequency (N)	Percentage (%)
Gender	Male	46	53.5
	Female	40	46.5
Gestational age	< 30 weeks	9	10.5
	30 to 32 weeks	34	39.5
	>32 weeks	43	50
Birth weight (In grams)	≤ 1500	63	73.3
	>1500	23	26.7
Mode of delivery	LSCS	37	43
	Labour natural	49	57
Singleton/twin	Singleton	72	83.7
	Twin	14	16.3
Oxygen supplementation	Present	66	76.7
	Absent	20	23.3
Mode of supplementation	CPAP	53	80.3
	Nasal prongs	4	6.1
	Hood	9	13.6
Days of oxygen supplementation	< 5	36	54.5
	≥5	30	45.5
Complications	Respiratory distress syndrome	52	60.5
	Sepsis	24	27.9
	Exchange transfusion	27	31.4
	Phototherapy	33	38.4
	PDA	7	8.1

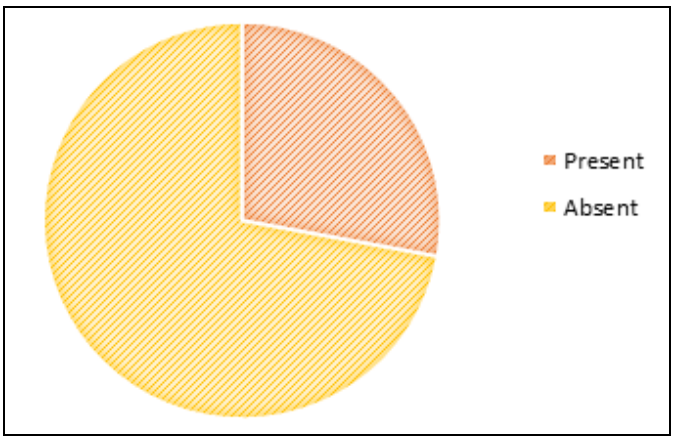

Fig 1: Pie chart showing distribution according to the presence of retinopathy of prematurity.

Out of the 86 study participants, 53.5% were male 46.5% were female. Most of the mothers, 50% of the participants belonged to gestational age of >32 weeks followed by 39.5% mother had gestational age of 30-32 weeks, 10.5% had gestational age of <30 weeks. Majority of the child, 73.3% were weighted less than or equal to 1500 grams and

26.7% were >1500 grams. Most of the participants' mothers, 57% had normal delivery and majority, 83.7% of the mother had singleton delivery. Among participants, 76.7% required oxygen supplementation, majority 80% were given oxygen supplementation through CPAP and 54.5% of participants received oxygen supplementation< 5 days. Among infants with complications, most of the child, 60.5% had respiratory distress syndrome followed by 38.4% required phototherapy and 31.4% required exchange transfusion. (Table 1)

Table 2: Association between risk factors and the occurrence of ROP

Variable		Retinopathy of prematurity				X^2	P value
		Present		Absent			
		N	%	N	%		
Gender	Male	12	26.1	34	73.9	0.163	0.687
	Female	12	30	28	70		
Birth weight (In grams)	>1500	09	21.9	32	78.1	12.77	0.001
	≤ 1500	15	23.8	48	76.2		
Gestational age	< 30 weeks	8	88.9	1	11.1	20.83	0.001
	30 to 32 weeks	10	29.4	24	70.6		
	>32 weeks	6	14	37	86		
Mode of delivery	LSCS	8	21.6	29	78.4	1.275	0.256
	Labour natural	16	32.7	33	67.3		
Singleton/ twin	Singleton	19	26.4	53	73.6	0.507	0.477
	Twin delivery	5	35.7	9	64.3		
Oxygen supplementation	Present	22	33.3	44	66.7	4.154	0.042
	Absent	2	10	18	90		
RDS	Present	21	40.4	31	59.6	10.17	0.001
	Absent	3	8.8	31	91.2		
Sepsis	Present	14	58.3	10	41.7	15.31	0.001
	Absent	10	16.1	52	83.9		
Exchange transfusion	Present	16	59.3	11	40.7	19.22	0.001
	Absent	8	13.6	51	86.4		
Phototherapy	Present	7	21.2	26	78.8	1.193	0.275
	Absent	17	32.1	36	67.9		

Table 2 shows association between risk factors and the occurrence of ROP. Among infants with birth weight less than or equal to 1500 grams, 23.8% had ROP and 76.2% did not have ROP whereas among infants with birth weight >1500 grams 21.9% had ROP and 78.1% did not have ROP and this difference in occurrence of ROP between different weight categories was statistically significant (P< 0.001%). Among infants whose mother had gestational age <30 weeks, 30-32 weeks and >32 weeks 88.9%, 29.4% and 14% had ROP respectively and this occurrence of ROP between different weeks of gestational age of the mother categories was statistically significant (P<0.001%). Out of the 86 study participants, 33.3% infants who received oxygen supplementation had ROP and 66.7% did not have ROP, whereas 10% of infants who did not receive oxygen supplementation had ROP and 90% did not have ROP and this occurrence of ROP in Oxygen supplementation category was statistically significant (P<0.001%). Among the study infants who had sepsis 58.3% had ROP and 41.7% did not have ROP, whereas in infants without sepsis 16.1% had developed ROP and 83.9% did not have ROP and this difference was statistically significant (P<0.001%). In the study participants who received exchange transfusion 59.3% had developed ROP and 40.7% did not develop ROP, whereas infants who did not receive exchange transfusion 13.6% developed ROP and 86.4% did not develop ROP and this was statistically significant (P<0.001%). Other variables like phototherapy, mode of delivery and twin delivery were not statistically significant.

Discussion

Retinopathy of prematurity is a disorder of the developing retinal blood vessels in the premature infant retina. The key pathological change is local ischemia with subsequent peripheral retinal neovascularization. This may regress completely or leave sequelae from mild myopia to bilateral total blindness. The present study was a descriptive study carried out in the department of ophthalmology, Rajah Muthiah Medical College and Hospital, Chidambaram among infants born in the hospital during the study period. The objective of the present study was to find out the incidence of retinopathy of prematurity and to identify the risk factors which predispose to the development and progression of ROP.

86 participants were recruited into the study. Out of which, 53.5% were males and 46.5% were females. 50% were born after 32 weeks of gestation and 39.5% were born after 30 to 32 weeks of gestation. 73.3% were born with birth weight of less than or equal to 1500 grams. 43% were born out of caesarean section and 57% were born out of natural labour. 83.7% were born out of singleton delivery. 76.7% had received oxygen supplementation. 80.3% had received oxygen through CPAP and 54.4% received oxygen for less than 5 days. 60.5% had respiratory distress syndrome. 38.4% had received phototherapy and 31.4% had received exchange transfusion. 39.5% had Premature rupture of membrane and 8.1% had maternal anaemia.

27.9% participants were found to be diagnosed with retinopathy of prematurity. Shrestha J *et al.* reported a similar proportion of ROP (29.5%) with regard to the present study [6]. Gu MH *et al.* reported the proportion to be 9.8% [7]. On the other hand Chen M *et al.* reported a higher proportion of ROP about 47% [8]. Kim SJ *et al.* in their major review reported that the risk of ROP varied widely across different populations across the globe. They also suggested understanding the predictors of ROP in each population separately [9].

Birth weight of less than 1500 grams was found to be

associated with the occurrence of ROP in the present study. Gestational age of less than 30 weeks was found to be associated with the presence of ROP. Seiberth V *et al.* reported a similar finding that the low gestational age was associated with the occurrence of ROP [10]. Mihara E *et al.* reported shorter gestational age as the risk factor for retinopathy occurrence [11]. Mutlu F and sarici S reported that by preventing preterm birth the incidence of ROP could be reduced [12]. Shrestha J *et al.* also reported a similar finding with regard to the gestational age [6].

Oxygen supplementation was found to be associated with the occurrence of retinopathy of prematurity in the present study. Presence of RDS was found to the associated with the presence of ROP in the present study. Lad EM *et al.* reported respiratory distress was significantly associated with the occurrence of retinopathy of prematurity [13].

The presence of sepsis was also found to be associated with the occurrence of ROP in the present study. Gu MH *et al.* reported a similar finding that presence of septicaemia had increased the chance of getting ROP to 2.88 times [7]. Chen M *et al.* in their study reported additive and multiplicative patterns of interaction between three risk factors namely, neonatal sepsis, oxygen exposure and low gestational age [8].

The presence of exchange transfusions was also found to be associated with the presence of ROP in the present study. Seiberth V *et al.* reported high volume of blood transfusion as a factor associated with the development of retinopathy of prematurity [10]. Shohat M *et al.* also reported the risk of ROP increase with number of blood transfusions received [14]

Conclusion

The prevalence of retinopathy of prematurity was found to be on the higher side in the study population. Lower birth weight, lower gestational age, presence of RDS, history of sepsis and exchange transfusions were found to be the risk factors associated with ROP.

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