INCIDENCE AND RISK FACTORS CONTRIBUTING TO ROP: STUDY FROM NEONATAL CARE UNIT- SOUTH INDIA

Karthiyaeni Mani[1], Sathya Jeganathan[2]

[1]Senior Resident, Department of Paediatrics, Chengalpattu Medical College Hospital, Chengalpattu.
[2]Professor, Department of Paediatrics, Chengalpattu Medical College Hospital, Chengalpattu.

ABSTRACT

The study was conducted to identify the incidence of retinopathy of prematurity among the preterm neonates treated at neonatal unit and to evaluate the associated risk factors for ROP.

DESIGN

Prospective observational study.

SETTING

Neonatal Intensive Care Unit (NICU) of Department of Paediatrics at Chengalpattu Medical College. During the study period, 159 babies were treated at the NICU and 111 babies were discharged from the unit. Among those babies who were discharged, 14 neonates were lost for followup for ROP screening. This lost to followup was 12.6% of the study population. In this study 97 infants were screened, out of which 18 infants had ROP. The rate of ROP is 18.6% in our institution and 2 out of 18 babies had threshold ROP (11.1%), who were treated with Laser therapy.

KEYWORDS

ROP, Preterm, South India.

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INTRODUCTION

The incidence of childhood blindness in world is 1.4 million, out of which 40% is preventable.[1] A 21% of blind children have retinal causes, of which Retinopathy Of Prematurity (ROP) figures very high. The incidence of retinopathy of prematurity in western countries in babies weighing <1000gm and 28 weeks is 40–60%, of which 5-10% requires laser therapy.[2] Indian literature reveals that the most important risk factors for ROP are prematurity and low birth weight.[3] Other factors include oxygen therapy, duration of ventilation, hypotension, sepsis, anemia, blood transfusion, apnea, antioxidant deficiency, hypoglycemia, patent ductus arteriosus, etc. Data about ROP in India are from level III units, not many studies are from rural or semi urban level II units. This study was conducted at this semi-urban neonatal nursery (level II) to find out the incidence and risk factors for retinopathy of prematurity.

METHODOLOGY

The study was conducted to identify the incidence of retinopathy of prematurity and to evaluate the associated risk factors for ROP among the preterm neonates treated at NICU (Neonatal Intensive Care Unit) at Chengalpattu Medical College and Hospital.

DESIGN

Prospective observational study.

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Corresponding Author:
Dr. Sathya Jeganathan,
Department of Paediatrics,
Chengalpattu Medical College Hospital,
Chengalpattu-603001.
E-mail: sathyaj65@gmail.com
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SETTING

Neonatal intensive care unit (NICU) of Department of Paediatrics at Chengalpattu Medical College and Hospital, South India.

DURATION

From November 2009-April 2010.

Study Population

All preterm babies treated at the NICU. Inclusion criteria.[4] (AIIMS GUIDELINES) Gestational age less than or equal to 32 weeks, birth weight less than or equal to 1500gm, babies with gestational age >32 weeks or birth weight >1500gm with significant neonatal course like respiratory distress syndrome, sepsis, multiple blood transfusions, apneic episodes, intraventricular haemorrhage and babies in whom gestational age could not be assessed. Study parameters included demographic factors like gestational age, gender, birth weight and risk factors for ROP like apnea, hypoglycemia, sepsis, ventilated period, seizures. All recruited preterm neonates were subjected for ROP screening as per the unit policy.

The screening was carried out in the new born unit at Chengalpattu Medical College Hospital by the ophthalmologist in the presence of neonatologist to handle any systemic complications. Examination was undertaken as per recommended standard guidelines. Data was collected using a pretested questionnaire and findings were documented. Followup of the neonates was as per the recommendations of the ophthalmologist. Study parameters were analysed among the group with and without ROP for statistical significance.

STATISTICS

Data analysis was done using SPSS 17.0 version. The data was analysed using contingency table analysis with Fisher's exact

test or Pearson x2 test with Cochran's test of linear trend for correction as indicated. Comparison between the groups with and without ROP was made using student's T test and chi square test. All variables that had significance on univariate analysis were subjected to a stepwise forward logistic regression analysis to determine the independent risk factors associated with ROP. A value of p <0.05 was considered as significant.

ETHICS

Study was conducted after Institutional ethical approval. Informed written consent was obtained from the caregivers-parents at the beginning of the study.

RESULTS

During the study period 159 preterm neonates were treated at the NICU, 111 were discharged from the unit and 48 preterm babies expired. Among those babies who were discharged, 14 children were lost for followup for ROP screening. Hence, the lost to followup was 12.6% of the study population; 97 babies completed the study after ROP screening. Gestational age ranged from 28 weeks to 32 weeks with a mean of 31.39+1.57 weeks (Fig 1). Gender distribution revealed the Male:female ratio to be 1:1. Among the study group 91 were AGA, 2 were SGA and 4 were LGA. Birth weight ranged from 1kg - 2.5kg with a mean of 1.57 + 0.26kg; 32% of the babies were very low birth weight babies; 43% of the babies were between 1.5 – 1.75kg.

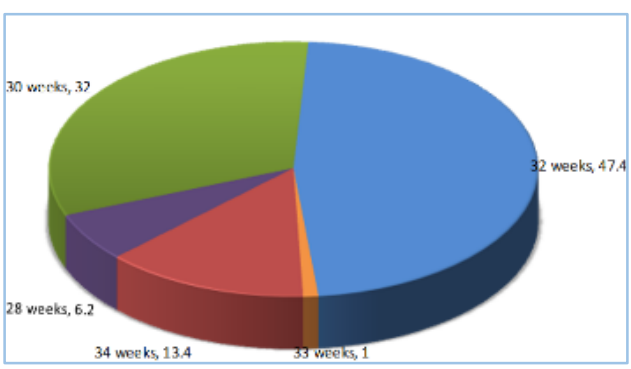

Fig. 1: Showing the gestational age of the study group

Of the 97 children who underwent ROP screening 18 were positive for ROP. None in the study group above 1750gm had retinopathy of prematurity. Univariate analysis of the study group revealed hypoglycemia, requirement of Fio2 more than 50, anemia Hb <10, use of blood component transfusion more than 10ml/kg were found to be significant. (Table 1).

Factors Under Study	95% Confidence Interval			
	P value	Odd Ratio	Lower	Upper
Hypoglycemia	0.007	5.692	1.443	22.459
Fio2>50	0.020	3.624	1.178	11.154
Anemia	0.036	4.229	1.008	17.732
Blood Component	0.001	5.900	1.957	17.785
Packed Cells	0.007	5.692	1.443	22.459
Transfusion (Ml/Kg)	0.002	5.692	1.443	22.459
Seizures	0.006	3.389	7.238	1.459
DVET	0.932	1.103	.116	10.503
Phototherapy	.279	3.045	.370	25.071
Fio2>80	0.506	1.469	.471	4.585
Oxygen/Vent	0.474	1.508	.488	4.660
Oxygen	0.474	1.508	.488	4.660
Hyperbilirubinemia	0.391	2.464	.295	20.588
Culture Negative Sepsis	0.182	2.133	.689	6.603
Culture positive Sepsis	0.502	2.265	.194	26.435
SURFACTANT	0.150	2.960	.638	13.741
APNEA	0.355	1.631	.576	4.620
TTNB	0.288	1.824	.597	5.574
RDS	0.555	1.375	.476	3.966
Abruption	.336	2.344	.395	13.914

Table 1: Showing the univariate analysis of significant factors

On the basis of the univariate analysis the following variables were selected for multivariate logistic regression analysis: (a) Hypoglycemia, b) Seizures, c) Fio2 >50, d) Anemia, e) Blood Component, f) Packed cells g) Transfusion (ml/kg) of these, the administration of Blood component [Adjusted Odds Ratio 11.0135, 95% Confidence Interval 1.2919 to 93.8938; (p = 0.0282)] Hypoglycemia [Adjusted Odds Ratio 5.5, 95% Confidence Interval 1.2394 to 24.3053; (p = 0.0249)] emerged as independent risk factors of ROP.

	HYPOGLYCEMIA		Total	P value	Odd Ratio		95% Confidence Interval	
	No	Yes					Lower	Upper
ROP	No	61	18	79	0.020	3.389	1.171	9.811
	Yes	9	9	18				
	Total	**70**	**27**	**97**				

Table 2: ROP & Hypoglycemia

There is a significant difference (p=0.020) in Hypoglycemia among ROP cases and non-cases.

Risk Factors	Odd Ratio	95% Confidence Interval		P value
		Lower	Upper	
Hypoglycemia	5.4885	1.2394	24.3053	0.0249
Seizures	3.7146	0.5224	26.4117	0.1898
Fio2>50	3.6459	0.9091	14.6213	0.0679
Anemia	0.8491	0.0437	16.5088	0.9140
Blood Component	11.0135	1.2919	93.8938	0.0282
Packed Cells	3.8597	0.2159	69.0099	0.3586
Transfusion (Ml/Kg)	0.8930	0.7446	1.0709	0.2221

Table 3: Showing the multivariate analysis

DISCUSSION

In our study 97 preterm neonates were screened, out of which 18 had ROP, the rate of ROP is 18.6% in our institution. Two out of eighteen babies had threshold ROP (11.1%) who were treated with Laser therapy. On univariate analysis the risk factors found to be significant in study were: (a) Hypoglycemia, b) Seizures, c) Oxygen therapy (Fio2 >50), d) Anemia, e) Blood component, f) Packed cells, g) Transfusion (ml/kg). Multivariate analysis showed hypoglycemia and blood component usage as significant factors.

According to the prospective observational study conducted by Sudha Chaudhri, et al.[5] at KEM Hospital Pune, out of 552 infants screened 123 (22.3%) had ROP. Septicemia, apnea, ventilation and use of blood products were found to risk factors.

Out of 123 infants with ROP, 41(33.3%) needed laser photocoagulation. A study conducted at University Medical College, GTB Hospital, Delhi by Gupta et al.[6] revealed Septicemia exchange transfusion, Hyaline membrane disease and Apnea as significant risk factor for ROP.

In their study, they screened babies with birth weight <1500gm and gestational age <35 weeks. Out of 60 infants, 12 babies had ROP (rate = 21.7%). Retinopathy was significantly more severe in babies with hyaline membrane disease and lower birth weight.

Reka et al.[7] conducted a prospective study at St. John's, Bangalore, in which 100 babies were screened. The rate of ROP in their study was 46%. In their univariate analysis, significant factors were gestation <32 wks., oxygen use, anemia, blood transfusions and apnea. Oxygen was one of the significant risk factors, but 33% of babies not on oxygen developed ROP. Multiple logistic regression analysis identified only presence of anemia and duration of oxygen therapy in days as significant risk factors for the development of retinopathy of prematurity. In this study, oxygen therapy was found to be significant on univariate analysis, but not on multivariate regression analysis. Similar to the study at Chengalpattu, hypoglycemia and blood component usage were found to be significant risk factors on multivariate regression analysis. This shows that apart from oxygen therapy, factors like anemia, hypoglycemia and blood component usage also influence the development of ROP.

In a prospective study conducted by Krishnamurthy et al.[8] 50 babies were screened for retinopathy of prematurity of which 12 babies had ROP. The rate was 24%. Oxygen administration and its duration was found to be a significant factor in the development of ROP. Apneic spells, hyaline membrane disease, short gestational period and exchange transfusions were significantly associated with increased risk of ROP.

Dutta et al.[9] conducted a case control study in babies who had Retinopathy of prematurity to analyse the risk factors for threshold ROP. Out of 108 babies with ROP, 53 babies had threshold ROP (T-ROP) and 55 babies had sub-threshold ROP (ST – ROP). On univariate analysis, packed cell transfusions for anemia, Double Volume Exchange Transfusions (DVET), number of DVET, ventilation, gestational age <28 weeks and apneic episodes were significantly higher in the T-ROP group. On multivariate analysis, the administration of packed cells [OR 2.8, 95% CI 1.2, 6.6; (p = 0.014)] and DVET [OR 2.7, 95% CI 1.2, 6.5; (p =0.022)] emerged as independent risk factors of T-ROP. Their study is comparable to this study, where in blood component usage is considered as a significant risk factor.

We also observed that 10 babies out of the 18 babies with ROP were larger babies with birth weight >1500gm. This is comparable to the retrospective study conducted by Anand et al.[10] at Postgraduate Institute. They analysed case records of babies with retinopathy of prematurity who attended retina clinic, in which he found that 11 babies with threshold ROP would have been missed if western guidelines were followed. He also concluded in his study that western guidelines need to be modified for screening babies in developing countries.

First Author Year	Screening Criteria	Incidence	Risk Factors
Chaudhari S 2009	Gestation ≤ 32 wk. or birth weight < 1500 g or additional risk factors	22.3%	Apnea, Septicemia and Oxygen therapy
Gupta VP 2004	Gestation <35 wk. or birth weight <1500 g	21.7%	Apnea, Septicemia and Oxygen therapy
Rekha S 1996	Gestation <35 wk. or birth weight <1500g	46%	Anemia, Oxygen Therapy
Krishna Murthy 2006	Gestational age <□34 week and/or birth weight of <□1750g	24%	Apnea, Oxygen therapy, Hyaline Membrane Disease, Exchange transfusion
Dutta S 2004	Gestation <32 wk. or birth weight <1700g or premature babies of any gestation who have received prolonged oxygen therapy (> 30 days)	Not Reported	Administration of packed cells and double-volume exchange transfusion
CMCH study	Babies with birth weight <1500g <□Babies born at ≤32 weeks of gestation <□Selected preterm infants with a birth weight between 1500 and 2000g or gestational age of more than 32 weeks with sickness	18.6%	Univariate: Hypoglycemia, seizures, o2 therapy, anemia, Blood component therapy and packed cells Multivariate: Hypoglycemia and Blood products

Table 4: Retinopathy of Prematurity – Studies from India

CONCLUSION

ROP is a preventable cause of retinal blindness.

Other study revealed prematurity and oxygen therapy found to be a significant risk factor for ROP, whereas in this study blood component usage and hypoglycemia influence the occurrence of ROP. Thus judicial use of blood products and hypoglycemia in a preterm should be avoided.

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