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Research Article

Predictors of Sight Threatening ROP in a Tertiary Care Hospital of Himachal Pradesh

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Abstract

Purpose: To study the incidence, patterns and risk factors of sight threatening ROP.

Methods: A hospital based prospective observational study was conducted from January 2019 to December 2019 at Indira Gandhi Medical College Shimla. 250 babies who fulfilled inclusion criteria's were examined by an ophthalmologist at 3 weeks postnatal age. Baseline factors, systemic risk factors, and pattern of ROP were noted. Factors associated with sight threatening ROP including Type-1 ROP, Stage IV and V, were analyzed**.**

Results: Out of 250 babies screened 13.6% babies developed any type of ROP. The incidence of sight threatening ROP was 9.2%.Out of 23 babies with ST- ROP Type -1 ROP was seen in 20 (86.95%) and advanced ROP (stage IV and V) in 3(13%). Mean gestational age, birth weight and duration of oxygen exposure for sight threatening ROP were 29.9 weeks and 1.23 kg, 23.83 ± 9.722 days respectively. Septicemia and respiratory Distress Syndrome found to be significant risk factors associated with ST- ROP. Late presentation was main cause of stage 4 and 5 disease.

Conclusion: Low birth weight, lower gestational age and duration of oxygen used were basic factors associated with development of ROP but risk factors like RDS and sepsis were found to be significant and independent risk factors for ST-ROP. These risk factors should be prevented or babies having these risk factors should be followed up regularly and treated effectively to stop the progression of disease.

Keywords: Sight Threatening-ROP; Respiratory Distress Syndrome; Septicemia

Introduction

ROP is now becoming a main cause of avoidable childhood blindness in India and other developing countries [1,2]. The cases of ROP is increasing in India because of increased neonatal care units and improved neonatal survival rate. Approximately 2 million newborn out of total 26 millions live birth are at risk of developing ROP [3]. Prematurity, low birth weight, suboptimal health care, and prolonged supplemental oxygen are well known risk factors for the development of ROP. Other neonatal risk factors associated with ROP are cyanosis, apnea, mechanical ventilation, intraventricular hemorrhages, seizures, transfusions, septicemia, in utero hypoxia, anemia, patent ductus arteriosus, and vitamin E deficiency. ROP is a self limiting disease and spontaneous regression do occurs in many neonates. Sight threatening ROP if remained untreated leads to severe sequelae and results in irreversible blindness as well as all the psychosocial, educational and economic implications [4]. Newborns who are at risk needs retina screening because up to 15% of them develop ST-ROP and need urgent laser treatment [5]. All babies at risk of ST-ROP should be screened and treated. Present study was conducted to find out the incidence and

various risk factors particularly associated with ST-ROP so that we can suspect and detect ST-ROP early, followed by urgent laser treatment to preserve the sight of babies.

Materials and Methods

A hospital based prospective observational study was conducted from January 2019 to December 2019 at Indira Gandhi Medical College Shimla. All babies with birth weight ≤ 2000 gms or gestational age less than or equal to 34 weeks of gestational age were screened at 3 weeks and bigger babies with an unstable course or who presented late, those whom screening was recommended by pediatrician were also enrolled in the study. Informed consent of parents was taken after explaining in detail about methods and procedures involved in the study in their own language. Ethical clearance was obtained. Baseline parameters, systemic risk factors, and pattern of ROP were noted.

Findings of ROP screening were noted as NO ROP, Non ST-ROP defined as not requiring treatment and ST-ROP cases defined as cases requiring treatment in the form laser or surgery. Subsequently NO ROP cases were compared with ST-ROP for risk factors analysis. ST –ROP constituted all babies of Type-1 ROP and all cases with Stage IV and V disease at the time of first screening.[6] ST-ROP were categorized further as classic ROP, APROP and advanced stage ROP. If ROP was not found at first examination, the infants were re-examined after every two weeks until vascularisation was complete. If ROP was found, the examinations were done weekly for stage1-2 disease and twice weekly for stage 3 disease. These neonates were followed up till vascularization was complete or diseases progressed treatable stage.

Statistical analysis

The data was analysed using statistical software SPSS version 20.0. Quantitative variables and qualitative variables were analyzed using student t test using chi square test respectively . The association between potential related risk factors with ST- ROP and NO ROP were studied through Univariate as well as multivariate analysis. In all the above test the "p" value of less than 0.05 was accepted as statistically significant and all the test used for analysis were two tailed.

Results

Total 250 neonates were screened in which 132 babies were male and 118 were females. Mean birth weight was 1.82 ± 0.65 kilograms and mean gestational age was 33.84 ± 3.35 weeks. The mean age at the time of first screening was 5.148 ± 4.23 (range 3–20 weeks). In all screened babies, ROP was seen in 34 (13.6%) babies. Timely screening, within 4 weeks of birth, was done in 247 (98%) babies.

Figure 1 and table 1 shows distribution and pattern of ROP among screened babies. In present study out of 250 babies screened NON ST- ROP was present in 11 (4.4%) and ST- ROP in 23 (9.2%) babies. Incidence of ST-ROP was 9.2% in the present study (Figure 1). Of these 11 NON ST-ROP cases 2 had stage 1 and 9 cases had stage 2 diseases in various Zone. Out of 23 ST- ROP, 20 cases had of Type -1 ROP (86.95%) while 3 (13%) cases had advanced stage ROP. In all 20 type-1 ROP cases, classical ROP was seen in only 4 whereas 16 had APROP disease. In these 4 classical ROP cases, 3 cases had stage 2 with plus disease in Zone 2 and 1 case had stage 3 with plus disease in Zone 2. Out of 34 ROP cases Sixteen (47%) were diagnosed as APROP with features of large avascular area, flat new vessels, intraretinal shunting, and plus disease located in zone I or posterior zone II. Three cases were diagnosed as advanced stage of ROP at the time of first screening, and all presented late between 10 and 20 weeks of age. Out of which 2 cases had stage 4 b disease and one case had cicatricial ROP.

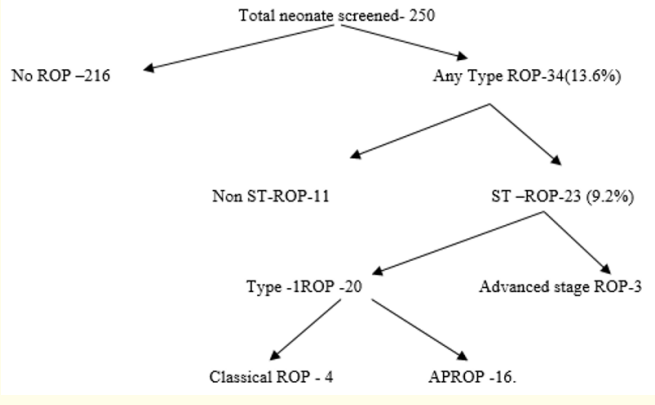

Figure 1: Flowchart showing distribution of ROP.

ROP stages							
ROP	NON-ST ROP-11		ST-ROP-23				Total
	Stage 1 Zone 2,3	Stage 2 Zone 2,3	Stage 3 Zone 2	Stage 4b	Cicatricial ROP	APROP Zone 2	
Number	2	9	4	2	1	16	34
	5.88%	26.47%	11.76%	5.88%	2.94%	47.05%	100%

Table 1: Pattern of ROP.

Table 2 Shows baseline characteristics of babies with NO ROP and ST-ROP.Mean birth weight was 1.91 ± 0.65 kilograms and 1.23 ± 0.33 kilograms respectively for NO ROP and ST ROP. This difference was statistically significant with P < 0.0001. The incidence of ST-ROP was inversely related to BW with babies weighing <1kg having the highest incidence of ST-ROP (72%). Mean GA was 34.45 ± 3.124 and 29.92 ± 1.6 weeks respectively for NO ROP and ST ROP. This difference was also statistically significant (P < 0.0001). Babies with a GA of <28 weeks had the highest incidence of ST-ROP (50%). Mean duration of oxygen exposure was 8.29 ± 11.26 and 23.83 ± 9.7 days respectively for NO ROP and ST ROP. This difference was statistically significant (P < 0.0001).

Base line Features	NO ROP	ST-ROP	P value
Cases(n) (239)	216	23	
Mean birth weight (Kg mean ± SD)	1.91 ± 0.65	1.236 ± 0.335	.0001
Mean GA(weeks, mean ± SD)	34.45 ± 3.124	29.92 ± 1.659	.0001
Time of presentation(weeks)	5.199 ± 4.38	5.31 ± 3.77	
Duration of O_2 Exposure (Days)	8.29 ± 11.267	23.83 ± 9.722	.0001
Birth weight			.000
<1kg (11)	3(27.27%)	8(72.72%)	
>1kg-1.5kg (93)	81(87.09%)	12(12.90%)	
>1.5kg-2kg (60)	58 (96.66%)	2(3.33%)	
>2kg (75)	74(98.66%)	1(1.33%)	
Gestational Age			.000
≤28 (4)	2 (50%)	2(50%)	
28-30 (28)	18(64.28%)	10(35.71%)	
30-32 (46)	36(78.26%)	10(21.73%)	
32-34 (45)	45 (100%)	0	
>34 (116)	115 (99.13%)	1(.86%)	

Table 2: Shows basics features of babies with NO ROP and ST-ROP.

Table 3 shows univariate analysis of the other risk factors for ST-ROP. There was a significant association between development of ST-ROP and risk factors like sepsis, surfactant used, RDS, apnea, anemia, thrombocytopenia, phototherapy, blood transfusion, multiple birth, antenatal steroid intake, premature rupture of membranes, congenital cardiac defects (p <.05) whereas antepartum hemorrhage ,gestational diabetes mellitus did not show any significant association with the development of ST-ROP. On multiple logistic regression analysis, only RDS and sepsis showed a statistically significant and independent risk factor for ST-ROP.

Risk factors (239)	NO ROP-216	ST-ROP-23	P value
Surfactant (13)	1(7.69%)	12(92.30%)	.000
RDS (57)	35(61.40%)	22(38.59%)	.000
Apnea (42)	30(71.42%)	12(28.57%)	.000
Sepsis (56)	35(62.5%)	21(37.5%)	.000
Anemia (44)	36(81.81%)	8(18.18%)	.03
Thrombocytopenia (5)	1(20%)	4(80%)	.000
Blood transfusion (44)	36(81.81%)	8(18.18%)	.03
Phototherapy (31)	19(61.29%)	12(38.70%)	.0001
CCD (3)	1(33.33%)	2(66.66%)	.0251
Multiple birth (25)	17(68%)	8(32%)	.0003
APH (2)	1(50%)	1(50%)	.1836
GDM (2)	1(50%)	1(50%)	.1836
ASI (8)	1(12.5%)	7(87.5%)	.0001
PROM (5)	1(20%)	4(80%)	.0003

Table 3: Univariate analysis of other risk factors for development ST- ROP (N = 239).

	B	S.E	WALD	df	Sig.	Exp(B)	95%C.I for Exp(B)	
							Lower	Upper
B.WT gms	-.002	.002	2.450	1	.118	.998	.995	1.001
GA wks	-.371	.236	2.474	1	.116	.690	.434	1.096
Oxygen duration	.033	.029	1.268	1	.260	1.034	.976	1.095
RDS	4.374	1.523	8.250	1	.004	79.374	4.012	1570.348
Sepsis	2.177	.920	5.595	1	.018	8.822	1.452	53.589
Constant	9.758	6.911	1.993	1	.158	17293.831		

Table 4: Multivariate Logistic Regression (N = 239).

Treatment was indicated in all 23 babies with ST- ROP. ILO was done in all 20 cases at our hospital and 3 cases with advanced stage were referred to higher centre. After laser treatment, babies were followed up till regression of ROP. All babies with stage 1and stage 2 diseases regressed without treatment.

Discussion and Conclusion

Despite all available treatments, ROP is still a major challenge as incidence of ROP is increasing with increased survival of premature infants. The overall incidence of ROP in the present study was 13.6% whereas incidence reported from previous studies in India range of 11.2%-47.3% [7-12]. This wide range of incidence showed that standard of neonatal care varies significantly in different parts of our country. However the incidence of ST- ROP in the present study was 9.2%.It was similar to studies reported by Hungi B., *et al*. [13] and Dwivedi., *et al*. [14]. Hungi B., *et al*. [13] and Dwivedi., *et al*. [14] have reported a incidence of 10.2% and 14.2% of severe ROP respectively. Incidence of ST-ROP in present study is higher than reported by kumar., *et al*. [7] and Vinkear., *et al*. [15]. They have reported 4.7% and 3.5% incidence of severe ROP respectively [7,15]. A bit higher incidence of ST-ROP (9.2%) in the present study from previous reported studies maybe due to high oxygen dose given to babies because of non availability of oxygen blenders in SNCU's.

In present study only 11% cases were of classical ROP whereas 47% cases were of APROP out of total ROP cases. The percentage of APROP cases is significantly higher than other studies. Kumar., *et al*. [7] have reported Zone I disease to be very uncommon with only one baby in their study. Hungi B., *et al*. [13] have reported 13.2% of ROP cases were APROP in a rural neonatal intensive care unit. The known risk factors for APROP includes prematurity, disruption of vasculogenesis, a low platelet count and supplemental unblended oxygen [16-19]. Duration of oxygen exposure was found to statistically significant risk factor for ST-ROP in present study. It is possible that early and excessive exposure to unmonitored oxygen therapy may lead to APROP-like pattern in these infants.

Mean birth weight and gestational age of ST-ROP cases in this study were 1.236 **±** 0.335 kg and 29.92 **±** 1.659 weeks respectively which were similar to reported by Kumar., *et al*. [7] (1113 ± 436 g and 29 ± 2.7 weeks, respectively). Low gestational age and lower birth weight were found to be significantly associated with ST-ROP in the present study and only 1 baby with ST-ROP have birth weight more than 2kg and GA more than 34 weeks. Study by Kumar., *et al*. [7] reported very few babies developing ST-ROP with gestational age more than 32 weeks and none with birth weight greater than 2 kg.

On univariate analysis risk factors like birth weight, gestational age, duration of oxygen exposure, sepsis, surfactant used, RDS, apnea, anemia, thrombocytopenia, phototherapy, blood transfusion, multiple birth, antenatal steroid intake, congenital cardiac defects, and premature rupture of membranes showed significant association for development of ST-ROP when compared to NO ROP but on multiple logistic regression analysis, only RDS and sepsis remained a statistically significant and independent risk factor for ST-ROP. It can be concluded from the present study that babies having RDS and sepsis were more prone to develop ST- ROP.

The lung diseases were an important risk factor for the development of both ROP. Neonates having lung diseases requires larger amount of supplemental oxygen, which is known cause of pathogenesis of ROP.[20] Study by Kumar., *et al*. [7] also found respiratory distress syndrome as significant factor associated with ST- ROP. The presence of sepsis has been associated with severity of ROP. The pathogenic microorganisms and their toxins cause damage in vascular endothelial cells, making WBC and platelets adhere to the blood vessel walls and form micro thrombi in the small blood vessels of the retina; these micro thrombi lead to blood vessel obstruction. Finally , an area of retinal non-perfusion forms, or a previously formed area expands [21]. Study by Dwivedi., *et al*. [14] found BW, GA, and age of presentation as significant risk factors for development of ST-ROP which was different from our study because they used Mild ROP as controls while this study used NO ROP as controls.

Treatment for ROP was carried out in 23 (9.2%) babies out of total babies screened. This is lower than 26%-75% reported in previous studies [8-10,13]. This reveals the lower incidence of severe ROP (9.2%) in this cohort. This can be attributed to better facilities and improved neonatal care, as our study was conducted in hospitals located within the city compared to studies from NICUs in rural areas.

The limitation of this study was inclusion of NICU from urban area only. Further studies are needed to include NICU's from rural area to find out other risk factors associated with disease.

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