Retinopathy of Prematurity in Tertiary Care Hospital

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ABSTRACT

AIM: To find out the incidence of retinopathy of prematurity in neonates in a tertiary level Neonatal Intensive Care Unit (NICU). Objective: Identify the risk factors for retinopathy of prematurity.

MATERIAL AND METHODS: Observational hospital-based study. After clearance from Institutional Ethics Committee, neonates who were admitted in NICU during the period of 1st October 2016 to 30th September 2018 were screened for ROP. Details of the antenatal history, perinatal risk factors, and the predisposing risk factors for the ROP were noted in the predefined proforma along with detailed treatment history. Local eye examination was done by a single specialized retinal surgeon.

Results and Observation: Of the total 115 enrolled neonates, 72 were males and 43 were female babies. 6 were ELBW, 29 were VLBW and 63 were LBW babies. 80 were preterm and 35 were term babies. The incidence of ROP was 26.96%.

Conclusion - Prematurity and low birth weight were the most significant risk factors for ROP. The other independent risk factors for ROP were oxygen therapy (90.32%), RDS (87.10%), sepsis (48.39%), and blood transfusion (25.81%).

KEYWORDS: ROP, prematurity, sepsis, oxygen therapy.

1. INTRODUCTION

Retinopathy of prematurity (ROP) is a disease process mostly seen in preterm neonates. ROP has a wide spectrum, ranging from mild, transient changes in the retina with regression to severe progressive vasoproliferation, scarring, detachment of retina, and blindness. In 1942, Terry first described ROP as retrolental fibroplasia with implication of oxygen therapy as the causative agent.[1]

Recent advances in neonatal care in the last decades have improved the survival rates for premature infants. Consequently, the incidence of ROP has increased in parallel to this. ROP is an important cause of childhood blindness in both developed and developing countries. ROP is a leading cause of childhood blindness which is preventable in middle-

income countries.[2]Recent studies from India report incidence of ROP ranging from 20% to 46%.[3]

Retinopathy of prematurity is a multi-factorial vasoproliferative retinal disorder. Three factors low gestational age, low birth weight, and prolonged exposure to supplementary oxygen following delivery have shown consistent and significant association with ROP.[2]

Other risk factors include shock, sepsis, apnoea, blood transfusion, exchange transfusion, hypoxic ischemic encephalopathy (HIE), anaemia, babies on mechanical ventilation for a longer duration, intraventricular haemorrhage (IVH), necrotizing enterocolitis (NEC), and birth asphyxia.[2]

Some researchers have suggested that those full-term infants with high-risk factors such as low birth weight, respiratory distress syndrome (RDS), oxygen administration may be at risk of developing retinopathy.4

2. AIM AND OBJECTIVE

AIM: To find out the incidence of retinopathy of prematurity in neonates in a tertiary level Neonatal Intensive Care Unit (NICU).

OBJECTIVE: Identify the risk factors for retinopathy of prematurity.

3. METHODS

STUDY DESIGN: Observational hospital-based study.

STUDY PERIOD: This study was conducted from 1st October 2016 to 30th September 2018 in a tertiary care centre.

STUDY SAMPLE: This study is time-bound for 24 months only. All newborns admitted at tertiary level neonatal intensive care unit who were screened for ROP were included in the study.

METHODOLOGY

After clearance from Institutional Ethics Committee, neonates who were admitted in our setup during the period of 1st October 2016 to 30th September 2018 and screened for ROP were enrolled in the study with due consent. Details of the antenatal history, perinatal risk factors, and the predisposing risk factors for the ROP were noted in the predefined proforma along with detailed treatment history.

Local eye examination: (done by a single specialized retinal surgeon)

The first screening was carried out in NICU not later than 4 weeks of age or 30 days postnatal under all aseptic precautions and following standard ROP screening guidelines. Infants <28 weeks or <1200 grams birth weight were screened early at 2-3weeks of age to enable early identification of Aggressive posterior ROP (AP-ROP). Subsequent examinations were done at 2-3 weeks intervals or even earlier, if necessary till the retina is fully vascularised. Classification of ROP was done according to the International classification (ICROP). The babies were swaddled and preferably fed one hour prior to examination. 30 minutes prior to the examination, the pupils have dilated with commercially available Tropicacyl Plus (0.8% Tropicamide + 5% Phenylephrine) eye drops in 1:1 dilution using methylcellulose eye drop so as to get 0.4% tropicamide + 2.5% phenylephrine. Excess drops spilling over were wiped with sterile cotton to prevent

systemic complications. The examination was carried out under topical anesthesia without any sedation using an indirect ophthalmoscope (HEINE Company with serial number 1170193) and a Volks +20 D condensing lens.

ETHICAL STATEMENT

Ethical clearance was obtained from an ethical review board NKPSIMS &LMH &Research Centre, Nagpur. The case file information was identified during data collection and was coded.

STATISTICAL TECHNIQUES USED:

The obtained data will be statistically analysed by applying descriptive (Average, percentile, mean,) of the significance of mean differences in terms of various variables. We will enter all data and further Statistical Analysis will be done with the help of SPSS-24 software.

4. RESULTS

Table 1: Gender distribution of neonates screened for ROP

Gender	No.	%
Male	72	62.6
Female	43	37.4
Total	115	100

Table 1 gives the gender distribution of neonates included in the study. Out of 115 neonates, 72 (62.6%) were males while 43 (37.4%) were females.

Table 2: Distribution of neonates according to weight

Weight (gm)	No.	%
ELBW: < 1000	6	5.22
VLBW: 1001-1499	29	25.2
LBW: 1500 – 2499	63	54.8
Normal:> 2500	17	14.8
Mean	1797.13	
SD	569.77	
Median	1700.00	

ELBW: Extremely low birth weight; VLBW: Very low birth weight; LBW: Low birth weight

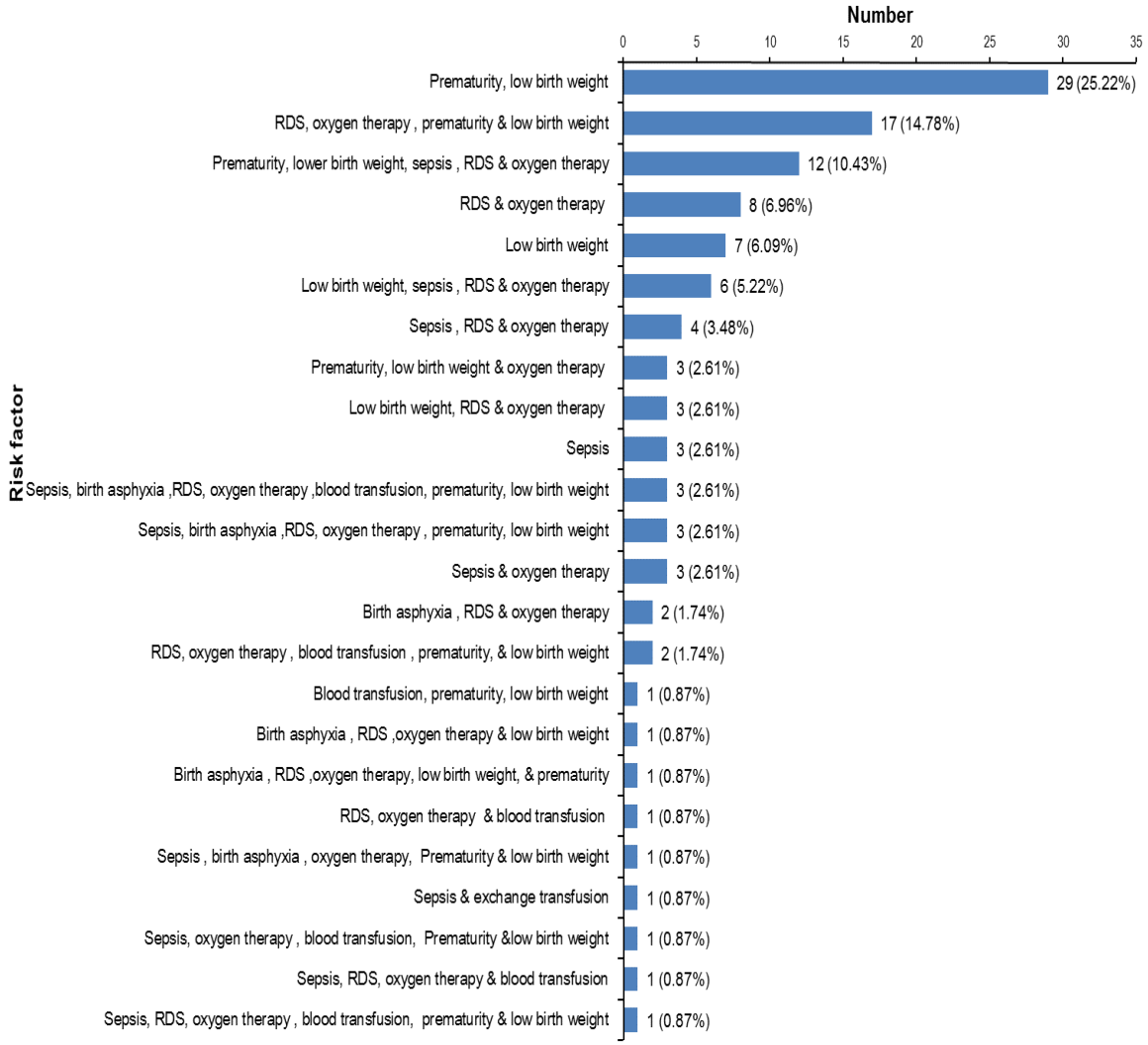
Table 2 provides the distribution of neonates according to weight in grams. Out of 115 neonates, 63 (54.8%) were in the range 1500 – 2499gm., followed by 29 (25.2%) in the 1001 – 1499gm category. There were 6 (5.22%) cases in the less than 1000gm category, while 17 (14.8%) were in the > 2500 gm category. The mean weight of neonates was 1797.13 gm with a standard deviation of 569.77 gm and a median of 1700 gm.

Table 3: Distribution of neonates according to gestational age

Gestational age	No.	%
Preterm	80	69.57
Term	35	30.43
Total	115	100

Table 3 provides the distribution of neonates according to gestational age. Out of 115 cases, 80 (69.57%) were preterm and 35 (30.43%) were term.

Figure No.1 - Risk factors for the development of ROP



This figure gives the distribution of neonates according to risk factors of ROP. There were a maximum of 29 (25.22%), neonates, with two risk factors prematurity and low birth weight. This was followed by 17 (14.78%) neonates with RDS, oxygen therapy, prematurity, and low birth weight. There were 12 (10.43%) cases having prematurity, lower birth weight, sepsis, RDS, and oxygen therapy as combined risk factors. RDS and oxygen therapy were risk factors only for 8 (6.96%) neonates, while 7 (6.09%) cases with exclusively low birth weight cases. Sepsis, low birth weight, RDS, and oxygen therapy

were observed in 6 (5.22%) of the cases. Other combinations of risk factors were observed in less than 5% of the cases.

Table 4: Risk of ROP associated with different factors

Factor	ROP Outcome		Odds ratio	95% C. I.		P-value
	No (n=84)	Yes (n=31)		Lower limit	Upper limit	
Gender						
Female	33 (39.29)	10 (32.26)	1.000			
Male	51 (60.71)	21 (67.74)	1.347	0.569	3.354	0.489 (NS)
Birth weight in kg	1.93±0.57	1.44±0.40	0.107	0.032	0.362	**< 0.0001 (S)**
Gestational age						
Term	31 (36.90)	4 (12.90)	1.000			
Preterm	53 (63.10)	27 (87.10)	3.801	1.318	14.159	**0.013 (S)**
Sepsis						
No	61 (72.62)	16 (51.61)	1.000			
Yes	23 (27.38)	15 (48.39)	2.463	1.041	5.867	**0.034 (S)**
RDS						
No	46 (54.76)	4 (12.90)	1.000			
Yes	38 (45.24)	27 (87.10)	7.807	2.735	28.962	**< 0.0001 (S)**
Birth asphyxia						
No	79 (94.05)	26 (83.87)	1.000			
Yes	5 (5.95)	5 (16.13)	3.003	0.753	12.007	0.086(NS)
Oxygen therapy						
No	40 (47.62)	3 (9.68)	1.000			
Yes	44 (52.38)	28 (90.32)	8.022	2.562	36.933	**0.0002 (S)**
Blood transfusion						
No	82 (97.62)	23 (74.19)	1.000			
Yes	2 (2.38)	8 (25.81)	13.169	2.969	101.200	**< 0.0001 (S)**

S: Significant, NS: Not Significant

Table 4 gives the risk of ROP associated with different factors. As regards gender, the risk of ROP is 1.347 [95% CI: 0.569 – 3.354] times higher in males as compared to females, although statistically insignificant (p=0.489). Odds associated with birth weight are 0.107 [95% CI: 0.032 – 0.362] indicating that lower birth weight increases the risk of ROP significantly with a p-value < 0.0001. Further, prematurity significantly increases the risk of ROP by 3.801 [95% CI: 1.318 – 14.159] times as compared to full term babies, with a p-value of 0.013. Presence of sepsis significantly increases the risk of ROP by 2.463 [95% CI: 1.041 – 5.867] times with a p-value of 0.034 as compared to those without sepsis. Neonates with RDS have increased risk of ROP of 7.807 [95% CI: 2.735 – 28.962] times with a p-value < 0.0001 as compared to those without RDS. Oxygen therapy

increases the risk of ROP by 8.022 [95% CI: 2.562 – 36.933] times with a p-value of 0.0002 as compared to those without the need of therapy. Further, blood transfusion increases the risk of ROP by 13.169 [95% CI: 2.969 – 101.2] as compared to those not requiring transfusion with a p-value < 0.0001.

5. DISCUSSION

ROP is a vasoproliferative disorder of immature retina affecting the vast majority of preterm newborns. The incidence of severe ROP in very preterm infants weighing <1250 gm could be as high as 37%. Low birth weight and prematurity are strongly associated with increased risk for the disease. ROP is currently the biggest contributor to infant blindness in developed and developing countries, as vision loss occurs secondary to retinal detachment that may occur in the most severe cases. In addition, myopia, strabismus, and amblyopia also occurs frequently.[5]

The pathogenesis of ROP is multifactorial: Besides prematurity and low birth weight, factors such as high-concentration oxygen therapy, sepsis, blood transfusion, IVH, NEC, PDA, suboptimal postnatal nutrition could put infants at significant risk for this devastating eye disease as established by clinical studies.[5]

"Analysis of prenatal and postnatal risk factors of ROP in a tertiary care hospital" was studied by Krishna A Rao et al[6] where they found an incidence of 21.6% while that of severe ROP was 6.7% which matches well with our incidence of 26.96%. They also found LBW and prematurity as most important risk factors for developing ROP and IVH as an independent risk factor similar to our study where we also found LBW and prematurity as risk factors for ROP whereas sepsis, oxygen therapy and blood transfusion were found to be an independent risk factors.

"A study of incidence and risk factors of ROP in NICU" in Egypt was studied by Abdel Hakeem et al[2] found an incidence of 19.2% which is slightly lower than our incidence probably because of their large sample size than our study. When divided as per stages of ROP, their incidence for stage I was 54.5% as compared to 32.26% in our study, 27.3% for stage II and 58.06% in our study, 18.2% for stage III and was 9.68% in our study. They did not find any babies in stage IV or V which goes with our study as we also did not find any babies with stage IV or V. They found low gestational age, sepsis, oxygen therapy and frequent blood transfusion as significant risk factors which match with our study.

Sudha Choudhari et al[1] studied "The incidence of ROP in a tertiary care centre" and the incidence they found was 22.3% which is similar to our incidence. They found no cases of ROP in babies weighing more than 2 kg and with a gestational age more than 36 weeks. This was not the case in our study where we found 14(45.16%) babies with ROP in the birth weight band of (1.5-2.5kg). We did not find a single case of ROP in babies weighing >2.5 kg.

Tae- im Kim et al[7] studied "Postnatal risk factors of ROP" and found an incidence of 20.7% which is a bit lower than our incidence of 26.96%. They found a gestational age <28 weeks, birth weight <1000gms to be the most significant risk factors with ventilator care for >48 hrs, apnoea and use of surfactant as an independent risk factors which does not match with our study. This probably could be attributed to better knowledge of ventilator

and upgrading of ventilator technology. We found prematurity, LBW, sepsis, oxygen therapy, RDS, blood transfusions as the risk factors in our study.

P. Manzoni et al[8] studied "Sepsis (fungal and bacterial) in VLBW preterm in relation to ROP" and found an incidence of 31.9 % as compared to 26.96% in our study. Sepsis as a risk factor gave a ROP incidence of 48.39% in our study as compared to 52.1% combining bacterial and fungal sepsis in their study.

Mitsiakos G et al[9] studied "Incidence of ROP in infants <32 weeks". Overall incidence of ROP in this study was 15.6% being much lower than our study probably because of the inclusion criteria of the babies <32 weeks. Their predisposing risk factors matched well with our risk factors being LBW, prematurity, oxygen therapy, RDS and sepsis.

Tian Wu et al[10] studied "The incidence of perinatal risk factors among VLBW infants in regard to ROP". Their overall incidence of ROP matched well with ours (26% vs. 26.96%) respectively. Percentage of babies in stage I,II,III in this study were 17.5%, 5.4%, 3.2 % respectively whereas in our study were 32.26%, 58.06%, 9.68% respectively. The risk factors were comparable in both the studies being RDS, sepsis and blood transfusion.

Yu- Shu Liu et al[11] studied "Incidence, risk factors, treatment of ROP among VLBW infants" and found incidence of 92.7% which was probably higher because they undertook only VLBW and extreme premature babies which themselves are the major risk factors for ROP as compared to our study. Mean birth weight and mean gestational age was much higher than this study as our study included term babies as well. LBW and prolonged oxygen therapy were major risk factors which are also major risk factors in our study.

6. CONCLUSION

In the present study titled "Retinopathy of prematurity in a tertiary care centre",

We conclude that-

1) Total 115 neonates were screened for ROP during the period 1st October 2016 to 30th September 2018.
2) Amongst these 115 neonates, 31 had ROP which accounts for an incidence of 26.96% in our tertiary level NICU.
3) According to stages of ROP, 10 (32.26%), 18(58.06%), 3 (9.68%) cases had stage I, II, III ROP respectively.
4) AP-ROP was found in 11 (35.48%) cases.
5) Laser therapy was required in 17 (54.84%) neonates.
6) According to our study, prematurity and low birth weight were the most significant risk factors for ROP.
7) The other independent risk factors for ROP were oxygen therapy (90.32%), RDS (87.10%), sepsis (48.39%) and blood transfusion (25.81%).

7. LIMITATIONS

The results of our study are not without limitations. The Current Study was administered within a single hospital setting in an urban area and thus may not be generalizable to other facilities.

8. **FINANCIAL SUPPORT AND SPONSORSHIP**- The authors have indicated they have no financial relationships relevant to this article to disclose.

9. **CONFLICT OF INTEREST**- The authors declare that they have no conflict of interest.

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