ORIGINAL RESEARCH PAPER
Volume - 11 | Issue - 01 | January - 2022 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

A STUDY OF RETINOPATHY OF PREMATURITY IN A TERTIARY CARE CENTRE

Neonatology

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ABSTRACT

INTRODUCTION: ROP is now the foremost problem, especially in most developing countries in Asia, where the survival of very low birth weight babies has improved over the last decade. Potential risk factors for the development of ROP are low gestational age, low birth weight, prolonged oxygen exposure, mechanical ventilation, birth asphyxia, systemic infection, blood transfusion, intraventricular haemorrhage. Literature mentions prematurity as the most common cause for the development of ROP. As there are large number of premature births in our institute and paucity of studies at Government institutes of Central India, the intention of this study was to detect the incidence of ROP in our institute and the various risk factors contributing to the development of ROP, so that it will help to take precautionary measures to prevent the development of ROP in high risk neonates.

OBJECTIVE: To determine incidence and risk factors responsible for developing ROP in high risk neonates.

METHODS: All the eligible neonates admitted in NICU of Indira Gandhi Govt Medical College Nagpur were enrolled in this prospective observational study and all antenatal, perinatal and neonatal details were recorded and screening for ROP was done by indirect ophthalmoscopy at 3rd or 4th week of postnatal age and followed up till retinal vascularization was complete. Data was analysed statistically to find incidence and risk factors for ROP.

RESULTS & CONCLUSION: Out of 211 babies screened, 34 babies were found to have ROP that gives incidence of ROP in this study was 16.11% . Risk Factors for ROP found significant on univariate analysis were Low gestational age ≤32 weeks, Low birth weight ≤1.5kg, Respiratory distress syndrome, Apnoea and oxygen therapy ≥ 5 days. Chance of occurrence of ROP was also more with the presence of more number of neonatal risk factors.

KEYWORDS

INTRODUCTION

Retinopathy of prematurity (ROP), which was previously called as retrolental fibroplasia, is a vasoproliferative disorder of the retina.[1] ROP is now the foremost problem, especially in most developing countries in Asia, where the survival of very low birth weight babies has improved over the last decade because of the advancements in neonatal intensive care.[2] The World Health Organisation (WHO) programme of Vision 2020 targeted against ROP Mentioned that the incidence of ROP can be reduced by early screening and referral for treatment.[3]

Indian studies have reported the incidence of ROP in 20% to 52% of screened neonates[4] Incidence of ROP in developed countries ranges from 21% to 65.8% among low birth babies.[5] ROP is a multifactorial disease, according to various studies, and many of them have found association between ROP and a plethora of maternal and infantile risk factors.[6] ROP has been associated with low gestational age (<32 weeks), low birth weight (<1500g) and prolonged oxygen exposure. In addition, potential or confirmed risk factors include mechanical ventilation, birth asphyxia, systemic infection, blood transfusion, intraventricular haemorrhage.[7]

ROP that goes undiagnosed and untreated in youngsters can lead to blindness.Hence to prevent the adverse visual outcome and possible blindness, timely screening, and treatment of ROP is essential l.[8]

Literatures have mentioned prematurity as the most common cause for the development of ROP. As there are large number of premature births in our institute and paucity of studies in government institutes of Central India, the intention of this study was to know the incidence of ROP in our institute and the various risk factors contributing to the development of ROP, which will help to take precautionary measures to prevent the development of ROP in high risk babies.

MATERIALS AND METHODS

This prospective study was conducted in NICU, Department of Pediatrics, Indira Gandhi Govt. Medical College Nagpur, in collaboration with the Department of ophthalmology. Neonates admitted in NICU from October 2018 to October 2020 were enrolled according to predefined inclusion and exclusion criteria's. All neonates with gestational age <32weeks or with birth weight ≤ 1500g irrespective of risk factors and neonates with >1500g with risk factors like Neonatal apnea, respiratory distress syndrome, Neonatal sepsis, anemia, shock etc were enrolled, while neonates with congenital anomalies, genetic abnormalities & metabolic syndromes were excluded. The study was conducted after taking permission from the ethics committee of institute and informed consent was taken from parents/ guardians. Total 346 neonates were enrolled. During enrolment basic details of the baby like antenatal risk factors, birth weight, gestational age and clinical diagnosis etc were recorded . All babies got investigated and treated as per standard protocols. First Follow up was done at the time of discharge or at 2 weeks of post natal age whichever is earlier. Clinical details (birth asphyxia, Hyaline membrane disease, Apnea, Neonatal sepsis, Anemia, Shock , etc as well as treatment details (like receiving of Oxygen therapy, ionotropic support, blood transfusion, mechanical ventilation) were recorded.

Second Follow up was done at the time of scheduled ophthalmological screening, clinical as well as treatment details were updated. Scheduled ophthalmological screening as per NNF guidelines, was done at 4 weeks of age for neonates with gestation age more than 28 weeks (gestation age) or more than 1200 grams (birth weight) and at 3 weeks of age for neonates with gestation age less than 28 weeks (gestation age) or birth weight less than 1200 grams. Ophthalmological follow up was done till normal vascularization till the periphery. End point will be ROP or no evidence of ROP.

135 babies could not be screened due to loss of follow up. 211 neonates were followed up and the incidence of ROP among them as well as the risk factors predisposing for ROP were analysed

ROP was graded into zones and stages as per ICROP Classification. Data was analysed using SPSS statistical package. The incidence of ROP was calculated in simple proportion. Univariate analysis of risk factors for ROP was done by using the chi-squared test. A logistic regression model was performed to find independent risk factors for ROP which were shown to be significant on univariate analysis. A probability (p) of less than 0.05 was considered significant.

RESULTS

Out of 346 neonates enrolled we could follow up only 211 neonates

because of loss of follow up. The incidence of ROP in this study was 16.11% (34 neonates out of 211 screened neonates). Out of 34 babies with ROP, 15 babies (7.11%) had stage 1 ROP, 10 babies (4.74%) had stage 2 ROP , 7 (3.32%) babies had stage 3 and 2 babies had stage 4(0.95) ROP.

Among the 34 neonates who developed ROP, 28 neonates (82.35%) had ≥3 neonatal risk factors whereas 4 neonates (11.76%) had 2 risk factors and 2 neonates (5.88%) had only 1 risk factor. Hence the incidence of ROP was high with presence of more number of risk factors

The risk factors were assessed based on the Univariate analysis (Table 1) using presence or absence of ROP as outcome variable, **Low gestational age (≤32 weeks)** [OR=8.23; p <0.001], **low birth weight (≤1.5kg)**[OR=8.11; p value<0.001], **RDS** [OR=5.31; p value<0.001], **Apnoea**[OR=3.36; p value=0.0012] and **oxygen therapy ≥5 days**[OR=4.45; p value=0.0001] were found significantly associated with ROP.

On Multivariate logistic analysis of various risk factors which were significant on univariate analysis **low gestational age ≤32weeks** [OR=6.43; p value=0.0010] and **Oxygen therapy ≥5 days** [OR=3.82, p value=0.0080] were found to be the significant predictors affecting ROP in this study (table 2).

Risk factors	ROP				Odds Ratio	Lower CI	Upper CI	P Value
	Present		Absent					
	No[r]	%	No[r]	%				
Gestational age								
≤ 32	28	82.35	64	36.16	8.23	3.23	20.95	<0.001
>32	6	17.65	113	63.64				
Birth weight								
≤1500	30	88.24	85	48.02	8.11	2.74	24.00	<0.001
>1500	4	11.76	92	51.98				
Gender								
Male	16	47.06	105	59.32	0.60	0.29	1.27	0.1854
Female	18	52.94	72	40.68				
Birth asphyxia								
Yes	8	23.53	37	20.90	1.16	0.48	2.78	0.7321
No	26	76.47	140	79.10				
RDS								
Yes	23	67.65	50	28.25	5.31	2.41	11.69	<0.001
No	11	32.35	127	71.75				
Apnoea								
Yes	16	47.06	37	20.90	3.36	1.56	7.22	0.0012
No	18	52.94	140	79.10				

Table 1a: Univariate analysis of different risk factors with ROP

Risk factors	ROP				Odds Ratio	Lower CI	Upper CI	P Value
	Present		Absent					
	No[r]	%	No[r]	%				
Apnoea								
Yes	16	47.06	37	20.90	3.36	1.56	7.22	0.0012
No	18	52.94	140	79.10				
Sepsis								
Yes	24	70.59	143	80.79	0.57	0.24	1.30	0.1790
No	10	29.41	34	19.21				
Neonatal seizures								
Yes	2	5.88	30	16.95	0.30	0.06	1.34	0.0992
No	32	94.12	147	83.05				
Received Inotropes								
Yes	21	61.76	93	52.54	1.45	0.68	3.09	0.3232
No	13	38.24	84	47.46				
Blood transfusion								
Yes	9	26.47	47	26.55	0.99	0.43	2.28	0.9918
No	25	73.53	130	73.45				
Oxygen therapy								
≥5 days	25	73.53	68	38.42	4.45	1.96	10.10	0.0001
<5 days	9	26.47	109	61.58				

Table 1b: Univariate analysis of different risk factors with ROP

Risk factors	Beta	Standard error	Wald	P Value	Odds Ratio	Confidence interval
Gestational age (≤32weeks/>32weeks)	1.86	0.543	11.77	0.0010	6.43	2.22 to 18.60
Oxygen therapy (<5/≥5 days)	1.34	0.504	7.08	0.0080	3.82	1.42 to 10.27

Nagelkarke R^2=0.487; Hosmer lemeshaw test=0.010

Table 2: Stepwise Multiple logistic regression analysis of different risk factors with ROP

DISCUSSION

Retinopathy of prematurity (ROP) is a vasoproliferative disorder and among the preventable causes of blindness in children.

We enrolled 346 neonates who were admitted in NICU based on predefined inclusion and exclusion criteria. Ophthalmological screening was done during follow up in 211 babies. Out of these 34 neonates (16.11%) were found to have ROP. Out of 34 ROP cases detected, Stage 1 was seen in 15 cases (44.11%) Stage 2 was seen in 10 cases (29.41%), stage 3 was seen in 7 cases (20.58%), stage 4 was seen in 2 cases (5.88%) and stage 5 was not seen in study. The overall incidence of ROP in the present study was 16.11%

This was found similar to previous studies done by Shahidullah et al [9] and Sudha chaudhari et al [10] and the incidence of Retinopathy of prematurity was 23.7% and 22.3% respectively. Reddy B et al also found a similar result in 2016, incidence of ROP according to her study was13.5%. According to two major studies, CRYO-ROP [11] and ET-ROP [12], incidence of ROP were 65.8 % and 68 % respectively. Swarna Rekha and R.R. Battu [13] in their study, found that the incidence of ROP to be 46%. According to Charan R et al [4] the Incidence of ROP was 47% .

Among the 92 neonates with gestational age ≤32 weeks, 28 (30.43%) neonates developed ROP and 6 neonates (5.04%) who developed ROP were of gestational age >32 weeks. Incidence of ROP was more among neonates with low gestational age (≤32 weeks) than with gestational age >32weeks. It was consistent with the results of various indian and international studies. In a study done by Umamaheswari Balakrishnan et al[14] , Mean gestational age of neonates with ROP was 29.2±1.4 weeks and they concluded low gestational age as a significant risk factor for the development of ROP. Similarly in ETROP study [12] , the distribution of ROP was 89.00% of neonates with gestational age <27 weeks, 51.5% of neonates with gestational age 27 to 31 weeks and 14.2% in neonates with gestational age >32 weeks.

Out of 211 neonates 115 neonates were having birth weight ≤1.5kg, among them 30 (26.09%) neonates developed ROP whereas only 4 neonates (4.16%) among the 96 neonates with birth weight >1.5kg developed ROP. Thus Incidence of ROP were more among low birth weight (≤1.5kg) neonates than those with birth weight >1.5kg. Cryotherapy for Retinopathy of Prematurity (CRYOROP) [11] and ETROP [12] studies also reported more incidence of ROP among low birth weight babies i.e 65.8% and 68% respectively

In this study, among the 73 neonates with RDS, 23 (31.50%) neonates developed ROP whereas out of 138 neonates without RDS ,only 11 neonates (7.97%) developed ROP. It was concluded that the occurrence of ROP was higher in neonates with RDS. Similar results were found in study conducted by Ather M Taqui et al [15] and they concluded RDS as one of the risk factor for the development of ROP. In a study conducted by Deepali Gawai et al [16] , ROP was more in neonates with RDS than in neonates without RDS.

Among the 53 neonates with apnea, 16 (30.18%) neonates developed ROP, whereas only 18 neonates (12.85%) among 140 neonates without apnea developed ROP. Neonatal Apnea was found to have significant association with the development of ROP. This finding is also supported by M. Lakshmi Narayana Reddy et al [17] , also revealed a similar association between ROP and Apnea and In 2015 Shrutakirti Ghosh et al [18] also concluded that the Apnea increases the occurrence of ROP in neonates.

Among the 93 neonates who received oxygen therapy ≥5 days, 25

(26.88%) neonates have developed ROP, whereas only 7.62% (9 neonates) of neonates who did not receive oxygen therapy ≥5 days (34 neonates) developed ROP. It was determined from our study that the occurrence of ROP increases with prolonged oxygen therapy. Similar conclusion was made by Shah, V. A et al [19] in 2005 in their study on ROP.

Among the 34 neonates who developed ROP, 28 neonates (82.35%) had ≥3 neonatal risk factors, where as 4 neonates (11.76%) had 2 risk factors and 2 neonates (5.88%) had only 1 risk factor. Incidence of development of ROP is directly proportional to presence of number of risk factors, as we found the incidence of ROP was high in neonates with more neonatal risk factors. Similar result was found in previous studies done by Shrutakirti Ghosh et al and M.Lakshmi Narayana Reddy et al.

By univariate analysis it was found that low gestational age (≤32 weeks), low birth weight (≤1.5kg), RDS, apnoea, oxygen therapy >5 days were significantly associated with ROP. Upon applying multiple logistic regression analysis, low gestational age (≤32 weeks) and prolonged oxygen therapy (≥5 days) were found to be significant predictors for the development of ROP.

CONCLUSION

Out of 211 babies screened, 34 babies were found to have ROP that gives incidence of ROP in this study as 16.11% . Risk Factors for ROP found significant on univariate analysis were Low gestational age ≤32 weeks, Low birth weight ≤1.5kg, Respiratory distress syndrome, Apnoea and oxygen therapy ≥ 5 days. Chance of occurrence of ROP was also more with the presence of more number of neonatal risk factors. Low gestational age (≤32 weeks) and prolonged oxygen therapy (≥5 days) are significant predictors for the development of ROP.

Recommendations

As of now cases of ROP are at surge in India as result of increased survival of high risk neonates. Unregulated and inadvertent oxygen therapy, less awareness among paediatricians about saturation limits, increased ROP screening and death of expert ophthalmologists. There should be more emphasis on prevention of ROP by better neonatal care with judicious oxygen therapy and better ante natal care to prevent preterm births and low birth weight.

Limitation

We did enrol 346 neonates in our study but we could follow up only 211 babies because of loss of follow up of 135 neonates, which might have affected the results of the study.

We followed up the neonates till the ophthalmological screening, we did not include treatment and further complications of ROP

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