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TRENDS OF RETINOPATHY OF PREMATURITY IN A TERTIARY CARE CENTRE IN URBAN INDIA.

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ABSTRACT **Introduction:** Retinopathy of prematurity is the leading cause of preventable blindness in premature infants. Our study aims at finding the Incidence and severity of Retinopathy of prematurity (ROP) and its association with various risk factors like low gestational age, low birth weight, oxygen exposure, respiratory distress syndrome, sepsis, blood transfusion and intraventricular hemorrhage. **Methods:** This is a prospective observational study conducted in a tertiary care teaching hospital in Western Maharashtra. Patient data including systemic and ocular findings were documented. Incidence and severity of ROP was calculated and the association of various risk factors with ROP was calculated using Chi-square test. **Results:** Among the 266 babies included in study, the Incidence of ROP was found to be 13.50% and Type I disease was found in 1.31%. The mean birth weight of neonates with ROP was 1230.2 ± 479.5 g and the mean gestational age was 30.27 ± 2.87 weeks. Development of ROP was significantly associated with low gestational age (GA), low birth weight (BW) and Respiratory Distress Syndrome (RDS). **Conclusion:** Early screening of preterm babies is crucial for early diagnosis and treatment of ROP to prevent its sight threatening complications.

KEYWORDS : retinopathy of prematurity, incidence, severity, risk factors

INTRODUCTION:

Retinopathy of prematurity (ROP) is a major cause of preventable blindness in children worldwide (1). India accounts for the most preterm births in the world (3.5 million) [2] and the third highest incidence of LBW, with about 1.7 million weighing <2500 g and about 0.4 million <1500 g [3]. This predisposes India to be the hotspot for ROP.

ROP is a dynamic, time-bound disease that is not present at birth. The risk of severe, sight-threatening ROP can be reduced by quality improvement measures that reduce exposure to known risk factors such as poorly administered supplemental oxygen, sepsis and poor weight gain after birth. Early detection of ROP, followed by urgent laser treatment, is highly effective in preserving the sight of the babies [4].

Over the past decade, there has been an increase in proportion of ROP screening worldwide [5,6]. The exponential increase in services for preterm infants in India calls for an urgent need to expand ROP programs in facilities where the majority of preterm infants receive care. Three major programs cover the range of services for prevention of blindness from ROP in India. They are Child Health, Ministry of Health and Family Welfare; Rashtriya Bal Swasth Karyakram (RBSK) [7] and National Programme for Control of Blindness and Visual Impairment (NPCB and VI) [8].

Our hospital runs a Level III Neonatal Intensive Care Unit (NICU) where high quality care is provided to neonates with an aim of preventing the development of ROP among other life threatening complications. In collaboration with Ophthalmology department, strict ROP screening has been running in our hospital since many years where we strive for early detection and early treatment of ROP as per the ETROP guidelines [4].

Our study aims at finding the Incidence and Severity of ROP among the babies born at or admitted in our NICU. Among the various risk factors that are associated with the development of ROP, we have studied the association of gestational age, birth weight, oxygen exposure, respiratory distress syndrome, sepsis, blood transfusion and Intraventricular haemorrhage.

MATERIALAND METHODS:

The present study is a prospective observational study, carried out at the Department of Ophthalmology in Bharati Vidyapeeth Hospital, Pune, India. The study protocol was approved by the Institutional ethical committee {DCGI Reg no. - ECR 518/Inst/MH/2014/RR-17}. Informed and written consent was obtained from the mother of each neonate before enrolment.

A total of 266 preterm neonates were included and screened for retinopathy of prematurity, between the period of October 2019 to September 2021. All patients were recruited by randomised sampling method.

Inclusion criteria[9]:

Preterm neonates having either Gestational age at birth of less than or equal to 34 weeks; or Birth weight of less than or equal to 2000 grams; or those referred by Paediatrician irrespective of their Gestational age and Birth weight.

Study Procedure:

Initial examination was carried out at or before 30th day of life. All the preterm neonates fitting in the inclusion criteria were examined by the same ophthalmologist. A detailed history including birth weight, gestational age at birth and presence of risk factors under study during NICU stay was recorded. The pupils were dilated with combination of 0.4% tropicaimide and 2.5% phenylephrine eye drops. Screening was carried out with a binocular indirect ophthalmoscope and +20D lens in NICU/PICU and Retina Clinic room.

ROP was graded as per the International Classification of Retinopathy of Prematurity. Decision to treat the diagnosed cases of ROP was made according to the revised ETROP guidelines [4]. Both treated and untreated cases were followed up till ROP regressed.

Statistical analysis:

Data was collected and compiled in Excel sheet and was subjected to statistical analysis using Multivariate analysis. The SPSS version 27 was used for statistical analysis. For univariate analysis of qualitative data chi-square test was used. Also, Multivariate regression analysis was used to compute the relationship between the various risk factors and the severity of ROP. The p-value of <0.05 was considered significant.

RESULTS:

Among the 266 infants evaluated 163 (61.28%) were male and 103 (38.72%) were females. 36 infants (66 eyes) were diagnosed to have ROP with an incidence of 13.50%. 6 infants had only unilateral involvement.

Among the eyes of the newborns diagnosed with ROP, the eyes were

distributed according to stage of ROP. Majority of the eyes had Stage 2 disease (51.5%). Aggressive Posterior Retinopathy of Prematurity (APROP) was observed only in 2 eyes (3%) [Table 1]. The most prevalent zone involved was zone 3, in 491 (92.3%) infants, followed by zone 2, 35 (6.6%) infants and zone 1, in 6 (1.1%) infants.

The mean GA 32.67 ± 2.98 weeks (ranged from 25 to 40 weeks) and mean BW 1530.80 ± 480.84 g (ranged from 630 to 3555 g). The mean gestational age 30.27 ± 2.87 weeks and the mean birth weight 1230.2 ± 479.5 g of neonates with ROP was significantly on the lower side. We found significant association of gestational age (P<0.0002) and birth weight (P<0.0001) with ROP incidence. This indicates lower the birth weight and gestational age higher the incidence of ROP. The distribution of babies in various categories of GA and birth weight along with their association to occurrence of ROP is shown in [Table 2] and [Table 3] respectively.

[Table 4] shows association of ROP and various risk factors on univariate analysis. This association was studied by means of Chi-square test and p-value. We found statistically significant association between Respiratory Distress Syndrome and the development of ROP whereas oxygen exposure, sepsis, blood transfusion and intraventricular haemorrhage had no statistically significant association with incidence of ROP.

The multiple regression analysis of stage of the disease with the risk factors among the babies with ROP (n=36), gave the overall p value of 0.0091, indicating that there are 1 or more risk factors significantly associated with severity of the ROP. The regression equation depicted the statistically significant association of sepsis (p=0.0388) and IVH (p=0.0288) with the severity of ROP. The results of multiple regression analysis are indicated in [Table 5].

DISCUSSION

In this study, we screened preterm neonates for ROP as per the screening criteria defined by National Neonatology Forum of India. From a total number of 266 babies screened, ROP was diagnosed in 36 infants (66 eyes) with an incidence of 13.50%.

Several studies from India reveal a varied trend of incidence of ROP ranging from 18.50% to 41.5%. Our study shows a lower incidence when compared to that reported by Thakre S et al.[10] (27.73%), Goyal A et al.[11] (25.36%), Patel SS et al.[12] (24%) and Hungi B et al.[13] (41.5%). However, lesser incidences have also been reported from other Indian studies like Basani l, et al.[14] (2.3%). A high incidence of ROP was also reported in studies from Saudi Arabia [15] (38%), Taiwan [16] (45.8%) and Canada [17] (67%). Diligent screening and strict protocol following in our NICU has probably accounted for the low incidence, as other studies report lower incidence due to protocol. They attributed the high incidence rate to large sample size, longer duration of study or more survival of lower gestational age babies.

On assessing the severity of ROP, out of the 66 eyes diagnosed to have ROP, majority had Stage II ROP in 34 eyes (51%) followed by Stage I in 23 eyes (34%). Treatable ROP was found in 7 eyes (4 babies) with an incidence of 1.31%. Among the 7 eyes with treatable ROP, APROP was found in 2 eyes (28.57%). In Thakre S et al [10] study from Maharashtra, incidence of Type I ROP has been reported to be 11%. Other studies from various states in India report an incidence of treatable ROP to range from 2% [12] - 13.5% [18]. Middle Eastern counties have found treatable ROP in 3.7% [15] and reports from china show treatable ROP in 19% neonates [16].

While determining the association of Birth weight and Gestational age with ROP, we observed that the mean birth weight of neonates with ROP was 1230.2 ± 479.5 g and 13 babies (36%) had birth weight less than 1000 grams. The mean gestational age of neonates with ROP was 30.27 ± 2.87 weeks and 19 babies (53%) were between 27 to 31 weeks. We found a significant association of birth weight (P<0.0001) and gestational age (P<0.0002) with incidence of ROP. This was in line with other studies from Maharashtra [10], Gujarat [12], Madhya Pradesh [19], and West Bengal [20]. Studies by Al-Qahtani B et al. from Saudi Arabia [15], Freitas AM et al. from Brazil [21] and Fortes Filho J et al. from Southern Brazil [22] were in accordance with our study.

On assessing the association between oxygen exposure and ROP, we found positive correlation (Odds ratio- 1.53) between oxygen exposure and ROP, though statistically significant association (p=0.3654) was not found in univariate analysis. Similar positive association was found in other Indian and International studies by Thakre S from Maharashtra [10], Gupta VP from Delhi [23], Yang CY from Taiwan [16], Zepeda-Romero LC from Mexico [24].

While assessing the association between RDS and ROP, positive correlation was reported in our study between RDS and incidence of ROP (odds ratio 2.53) and on univariate analysis it was statistically significant (p=0.0390). This was in accordance with Indian studies like Thakre S from Maharashtra [10], Patel SS from Gujarat [12], Yelameli BC from Karnataka [18] and with International studies like Chang JW from Korea [25] and Akkawi MT from Palestine [26].

While assessing the association between sepsis and ROP, positive correlation (odds ratio= 1.80) was found between them, though no statistical significance was seen (p=0.1472) on univariate analysis. And on multiple regression analysis sepsis was significantly associated with severity of ROP (p=0.0388). This positive association between sepsis and ROP was found in almost all previous studies by Thakre S from Maharashtra [10], Patel SS from Gujarat [12], Yang CY from Taiwan [16], Hakeem AH from Middle East [27] and Khorshidifar M from Iran [28].

On determining the association between blood transfusion and ROP, we found positive correlation (Odds ratio- 2.23) between them, though not statistically significant (p=0.0618) on univariate analysis. Similar positive association was also found in Indian studies by Thakre S from Maharashtra [10], Patel SS from Gujarat [12], and other International studies by Hakeem AH from Middle East [27] and Khorshidifar M from Iran [28].

While studying the association between Intraventricular hemorrhage and ROP, positive correlation with Odds ratio of 1.70 was found between them but on univariate analysis, we did not find any statistically significant association. On multiple regression analysis, significant association was found in between IVH and severity of ROP. This positive association has been seen in other Indian study by Rao K [29] and International studies by Yang CY from Taiwan [16] and Freitas AM et al. from Brazil [21]

CONCLUSION:

We report low incidence and low severity of ROP on diagnosis in this study, which is probably attributed to good neonatal care, strict following of protocol, and robust screening program. The incidence of ROP in our study showed a positive association with low gestational age, low birth weight, oxygen exposure, RDS, sepsis, blood transfusion and IVH; reconfirming the role of these risk factors in the development of Retinopathy of Prematurity.

Limitation of the study is that we have considered limited number of risk factors that are commonly noted, for logistic reasons several other risk factors can also be included. Also a detailed study of NICU management protocols can be done.

Table 1: Distribution of eyes of newborns as per the stage of the disease:

ROP Stage	Stage I	Stage II	Stage III	Stage IV	Stage V	APROP
Frequency	23	34	3	1	3	2
Percentage	34.84	51.51	4.5	1.5	4.5	3

Table 2: Distribution of gestational age and its association with incidence of ROP:

Gestational age in weeks	ROP		Total	Chi-Square	p-value
	Yes	No			
25 – 26	2 (67%)	1 (33%)	3 (1.1%)	18.9752	<0.0002 *
27 – 31	19 (21%)	70 (79%)	88 (33%)		
32 – 33	8 (13%)	52 (87%)	59 (22%)		
>34	7 (6%)	110 (94%)	116 (43%)		

Table 3: Distribution of newborns as per the birth weight and its association with incidence of ROP:

Birth weight in	ROP		Total	Chi-Square Value	p-value
	Yes	No			
630 – 999	13 (50%)	13 (50%)	26 (10%)	34.36	<0.0001*

1500 –	10 (11%)	79 (89%)	89 (33%)		
>2000	3 (8%)	36 (92%)	39 (15%)		
1000 – 1499	11 (10%)	101 (90%)	112 (42%)		

Table 4: Association of various risk factors with incidence of ROP:

Risk Factors	Yes/No	ROP	No ROP	Odds Ratio	p-value
Oxygen Exposure	Yes	27	146	1.53	0.3654
	No	10	83		
RDS	Yes	27	132	2.53	0.0390
	No	8	99		
Sepsis	Yes	22	107	1.80	0.1472
	No	14	123		
Blood Transfusion	Yes	12	42	2.23	0.0618
	No	24	188		
IVH	Yes	14	65	1.70	0.2177
	No	21	166		

Table 5: Multivariate analysis of stage of ROP with its risk factors:

Variables	Coefficient	Std. Error	t	P
GA	-0.08839	0.05234	-1.689	0.0970
BW	-0.00004761	0.0003977	-0.120	0.9052
O2	0.3394	0.3090	1.098	0.2769
RDS	-0.2082	0.4277	-0.487	0.6284
SEPSIS	0.5925	0.2798	2.118	0.0388*
BT	-0.01619	0.3216	-0.0503	0.9600
IVH	-0.7046	0.3138	-2.246	0.0288*

REFERENCES:

1. Gilbert C, Foster A. Childhood blindness in the context of VISION 2020 – The Right to Sight Bull World Health Organ. 2001;79:227–32
2. Last accessed on 2019 May 21 Available from: https://www.who.int/news-room/fact-sheets/detail/preterm-birth
3. Last accessed on 2019 May 21 Available from: https://data.unicef.org/topic/nutrition/low-birthweight
4. Early Treatment for Retinopathy Of Prematurity Cooperative Group. Revised indications for the treatment of retinopathy of prematurity: Results of the early treatment for retinopathy of prematurity randomized trial. Arch Ophthalmol 2003;121:1684–94
5. Prakalapakorn SG, Greenberg L, Edwards EM and Ehret DEY. Trends in Retinopathy of Prematurity Screening and Treatment: 2008–2018. Pediatrics June 2021; 147(6)
6. Chuan Kang E, Lien R, Wang NK et al. Retinopathy of Prematurity Trends in Taiwan: A 10-Year Nationwide Population Study. Investigative Ophthalmology & Visual Science. July 2018;59:3599-3607
7. Rashtriya Bal Swasthya Karyakram.c2019. https://rbsk.gov.in/RBSKLive/
8. National program for blindness and visual impairment. c2019. https://npcbvi.gov.in/
9. Screening and management of Retinopathy of Prematurity. National Neonatology Forum, India. Jan 2020. Http://www.nnfi.org/assests/pdf/cpg-guidelines/ROP--Key%20Recommendations.pdf
10. Thakre S, Deshmukh P, Kalyanshetti G, Mishrikotkar J. Incidence, Severity, and Risk Factors of Retinopathy of Prematurity in Central Maharashtra, India. Perinatology 2017; 18(2):50-55
11. Goyal A, Giridhar A, Gopalakrishnan M, Thachil T. Neonatal Intensive Care Unit-based screening program for retinopathy of prematurity and its treatment in an Indian population. Indian J Ophthalmol 2019;67(6):828-833
12. Patel SS, Shendurnikar N. Retinopathy of prematurity in India: Incidence, risk factors, outcome and the applicability of current screening criteria. Int J Contemp Pediatr 2019; 6:2235-41.
13. Hungi, Bhavana et al. Retinopathy of Prematurity in a Rural Neonatal Intensive Care Unit in South India—A Prospective Study. The Indian Journal of Pediatrics 2012;79:911-915
14. Ayyala RS, Basani LB, Zurakowski D, et al. Retinopathy of prematurity: Incidence, prevalence, risk factors, and outcomes at a tertiary care center in Telangana. Journal of Clinical ophthalmology and Research 2016;4(3):119
15. Al-Qahtani B, Al-Otaibi M, Alabdulajabbar K, Selayem NB, Alshehri W, Omair A et al. Retinopathy of Prematurity Incidence and Risk Factors in a Tertiary Hospital in Riyadh, Saudi Arabia. Middle East Afr J Ophthalmol 2020; 26(4):235-239
16. Yang CY, Lien R, Yang PH, Chu SM, Hsu JF, Fu RH et al. Analysis of Incidence and Risk Factors of Retinopathy of Prematurity Among Very-low-birth-weight Infants in North Taiwan. Paediatrics & Neonatology 2011;52(6):321-326 78
17. Isaza G, Donaldson L, Chaudhary V. Increased incidence of retinopathy of prematurity and evolving treatment modalities at a Canadian tertiary centre. Canadian Journal of Ophthalmology 2019;54:269-274
18. Yelameli BC, Neelannavar RV, Das K. A study of risk factors and their correlation with severity of retinopathy of prematurity: a prospective study. Int J Contemp Pediatr 2020; 7:1984-90.
19. Dwivedi A, Dwivedi D, Lakhtakia S, Chalisgaonkar C, Jain S. Prevalence, risk factors and pattern of severe retinopathy of prematurity in eastern Madhya Pradesh. Indian J Ophthalmol 2019;67:819-23
20. Chattopadhyay MP, Pradhan A, Singh R, Datta S. Incidence and risk factors for retinopathy of prematurity in neonates. Indian Pediatr 2015; 52(2):157-8
21. Freitas AM, Mörschbächer R, Thorell MR, Rhoden EL. Incidence and risk factors for retinopathy of prematurity: a retrospective cohort study. Int J Retin Vitr 2018; 4:20 83
22. Fortes Filho J, Eckert G, Procianoy L, Barros CK, Procianoy RS. Incidence and risk factors for retinopathy of prematurity in very low and in extremely low birth weight infants in a unit-based approach in southern Brazil. Eye 2009;23:25–30
23. Gupta VP, Dhaliwal U, Sharma R, Gupta P, Rohatgi J. Retinopathy of prematurity — Risk factors. Indian J Pediatr 2004;71:887–892 86.
24. Zepeda-Romero LC, Lundgren P, Gutierrez-Padilla JA, Gomez-Ruiz LM, Quiles Corona M et al. Oxygen Monitoring Reduces the Risk for Retinopathy of Prematurity in a Mexican Population. Neonatology 2016;110:135-140 87
25. Chang JW. Risk factor analysis for the development and progression of retinopathy of prematurity. PLoS ONE 2019; 14(7): e0219934. 81 91.
26. Akkawi MT, Shehadeh MM, Shams ANA, Al-Hardan DM, Omar LJ, Almahmoud OH et al. Incidence and risk factors of retinopathy of prematurity in three neonatal intensive care units in Palestine. BMC Ophthalmol 2019; 19:189
27. Hakeem AH, Mohamed GB, Othman MF. Retinopathy of prematurity: a study of prevalence and risk factors. Middle East Afr J Ophthalmol 2012;19(3):289-94. 93
28. Khorshidifar M, Nikkhah H, Ramezani A, et al. Incidence and risk factors of retinopathy of prematurity and utility of the national screening criteria in a tertiary center in Iran. Int J Ophthalmic 2019;12(8):1330-1336
29. Rao, Krishna A; Purkayastha, Jayashree1; Hazarika, Manali; Chaitra, Raghuvamsi1; Adith, K Mithun Analysis of prenatal and postnatal risk factors of retinopathy of prematurity in a tertiary care hospital in South India. Indian Journal of Ophthalmology 2013; 61(11):640-644