A Longitudinal Study of Retinopathy of Prematurity at Great Eastern Medical School and Hospital, Srikakulam

Lakshmi Sativada[1], Dineshkanth Vudayana[2], Tejapraveen P.[3], Jogendra Prasad Behra[4]

[1, 2, 3, 4] Department of Ophthalmology, Great Eastern Medical School and Hospital, Ragolu Srikakulam, Andhra Pradesh, India.

ABSTRACT

BACKGROUND

Retinopathy of prematurity (ROP) is a vasculopathy affecting the premature retina. In India ROP is increasing due to the increased premature deliveries, well improved neonatal care and better neonatal survival rate. ROP screening by an experienced ophthalmologist plays an important role in screening, identifying and management of at-risk premature infants. Nowadays, the gold standard treatment is laser photocoagulation of avascular retina and anti-vascular endothelial growth factor (VEGF) depending on the severity of disease.[1]

METHODS

This observational study included 152 babies who were referred to the Department of Ophthalmology at Great Eastern Medical School (GEMS), Srikakulam for ROP screening. The screening of eyes was done with a binocular indirect ophthalmoscope with 20 D lens. Eyes were examined by application of topical anaesthetic drops after applying topical tropicamide drops till full dilatation was noted. ROP was staged and treatment was given accordingly.

RESULTS

Totally 152 infants were screened for ROP in the Department of Ophthalmology. Babies with gestational age between 26 weeks and 36 weeks were included in the present study. Babies with birth weight between 900 gm and 2000 gm were also included in the study. Of the 152 babies which were included in the study, 54 babies presented with different stages of ROP. The incidence of ROP in the present study was found out to be 35.5 %. When incidence of ROP was noted with respect to birthweight, in extremely low birth weight (ELBW) babies, incidence was found out to be 71.4 %; in very low birth weight (VLBW) babies incidence rate was found to be 48.4 %. When incidence of ROP was noted with respect to gestational age ROP incidence was found to be 65.2 % in babies with gestational age of < 32 weeks. There was no association with gender in the incidence of ROP. When ROP incidence was noted in babies who received O_2 therapy 59.2 % babies who received O_2 therapy developed ROP.

CONCLUSIONS

In our study, at our institute the incidence of ROP was 35.5 %. With appropriate screening for the babies at risk we can prevent the development of ROP and further complications. According to study results our recommendations are that initial screening should to be done as early as 4 weeks of postnatal age or 34 - 35 weeks post conceptional age and to be followed till term gestation. In the present study we found that usage of anti VEGF came out with promising outcome results. The procedure of anti VEGF was relatively safe and easy with a smaller number of complications when compared to laser photocoagulation.

KEYWORDS

Retinopathy of Prematurity, Laser Photocoagulation, Indirect Ophthalmoscope, Tropicamide, Anti VEGF

Corresponding Author:
Dr. Dineshkanth Vudayana,
Assistant Professor,
Department of Ophthalmology,
Great Eastern Medical School and Hospital, Ragolu Srikakulam - 532484,
Andhra Pradesh, India.
E-mail: aswinisativada@gmail.com

DOI: 10.18410/jebmh/2021/116

How to Cite This Article:
Sativada L, Vudayana D, Tejapraveen P, et al. A longitudinal study of retinopathy of prematurity at Great Eastern Medical School and Hospital, Srikakulam. J Evid Based Med Healthc 2021;8(11):593-596. DOI: 10.18410/jebmh/2021/116

Submission 06-10-2020,
Peer Review 12-10-2020,
Acceptance 18-01-2021,
Published 15-03-2021.

BACKGROUND

Retinopathy of prematurity is an important cause of preventable blindness in children, and it is believed to account for 6 - 18 % of childhood blindness in developed countries.[1] Recent advances in neonatal care in the last decade, have improved the survival rates for premature infants.[2] Consequently, the incidence of ROP has increased in parallel. ROP is under constant epidemiological study around the world.[3] Early identification of retinal damage and the institution of appropriate treatment prevent blindness and offer the child better overall development.[4]

In 1942, Terry found out this disorder and termed it as "Retrolental fibroplasia". Initially it was thought to be due to oxygen exposure. So, with restricted oxygen use, the incidence of ROP came down. With improvement of neonatal intensive care facilities, more and more premature infants are surviving and are more prone to develop ROP.[5]

Retinopathy of prematurity is a multifactorial vasoproliferative disorder of retina that increase in incidence with decreasing gestational age and birthweight. Three factors have shown consistence and significant association with ROP: low gestational age, low birth weight and prolonged exposure to supplementary oxygen following delivery.[6] The stages of ROP were described based on the the ophthalmoscopic findings at the junction between the vascularised and avascular retina; in stage 1 there is a faint demarcation line, in stage 2 is there is an elevated ridge, in stage 3 there is an extraretinal fibrovascular tissue, in stage 4 there is a subtotal retinal detachment, while in stage 5 there is a total retinal detachment. In addition, there is an entity known as plus disease, in which there is a significant vascular dilation and tortuosity which can be observed at the posterior retinal vessels, may be noted at any stage of ROP and it reflects the increased blood flow through the retina.[7]

The course of retinopathy of prematurity is, it resolves spontaneously depending on the stage of the disease or may resolve with treatment. Complications of ROP may vary from mild myopia to total blinding disease like retinal detachment. We wanted to identify some of the risk factors which are known to predispose ROP and to assess the progression of ROP in the examined cases. To analyse the outcome in the babies who received treatment.

METHODS

This is a longitudinal observational study conducted for a period of 18 months from October 2018 to March 2020 at Department of Ophthalmology, Great Eastern Medical School, Srikakulam, Andhra Pradesh. All preterm babies referred from paediatric department with birth weight < 1500 g and gestational age < 34 weeks were included in the study. Preterm babies having congenital retinal detachment were excluded from the study. Sample size was 152 babies based on the inclusion and exclusion criteria.

Screening Methods

The study was conducted with a sample size of 152 babies. The fundus examination of the eyes was performed with a binocular indirect ophthalmoscope. After instillation of topical anaesthesia drops, full dilatation was achieved by using topical tropicamide drops. Retinopathy of prematurity was divided into stages of the disease and zone involved as per the International Classification of Retinopathy of Prematurity (ICROP) classification guidelines. Those infants with ROP were examined every two weeks or weekly depending on the stage of the disease up to regression. Treatment modalities were considered for babies with stage III ROP with plus disease. Anti VEGF was considered for treatment for most of the infants as there were a greater number of infants in stage I ROP. It was relatively simple procedure and was done under aseptic precautions. In infants with severe ROP laser photocoagulation was done using green laser with the help of indirect ophthalmoscope. Over one session avascular retina was ablated with medium intensity burns followed by topical treatment with tobramycin eye drops. If skip areas were found, laser was repeated after one or two weeks. In some infants anti VEGF was given followed by laser depending on the stage of the disease and the area of avascular retina following anti VEGF. Infants with normal vascularisation till retinal periphery were not examined again.

Statistical Analysis

The results were tabulated, and statistical analysis was done using SPSS software and values were calculated using paired t test, Fishers two tailed test and chi square test.

RESULTS

Totally 152 infants were screened for ROP in the neonatal wards. The gestational ages of the infants were between 26 weeks to 36 weeks. Of the babies referred, 45.3 % (69) babies belonged to age group of < 32 weeks. The birth weights of the infants were in between 900 gms to 2000 gms. Of the 152 babies screened 105 (69 %) babies had birth weight of < 1.5 Kg. Of the 152 babies screened, 54 babies presented to us with some stages of ROP. Most of the babies, 24 (46.1 %) were in stage I of ROP. The incidence of ROP at our institution was found to be 35.5 %. Incidence rate of ROP among ELBW babies was found to be 71.4 %. Totally 46, among 95 VLBW babies developed ROP which shows an incidence rate of 48.4 %. Of the 152 babies presented, 80 (52.6 %) were males and 72 (47.3 %) were females. Out of males, 51.8 % presented with various stages of ROP and out of females, 47.3 % presented with various stages of ROP. There was no association for gender with the incidence of ROP. Of the 152 babies, 69 (45.4 %) babies received O_2 therapy out of whom 32 babies developed ROP.

Among 54 infants who developed ROP, 30 infants required anti VEGF treatment of whom 2 babies required second dose of anti VEGF and 2 cases required assisted laser photocoagulation treatment. 1 infant progressed to higher stages of ROP, i.e. there is a progression to retinal detachment. 8 babies underwent treatment with laser photocoagulation. In the present study there was no

significant association between O2 therapy and ROP (P = 0.0168).

Gestational Age	With ROP	Without ROP	Total	% of ROP
< 28 weeks	2	1	3	66.6 %
28 – 30 weeks	16	5	21	76 %
31 – 32 weeks	29	16	45	64.4 %
> 33 – 34 weeks	4	40	44	11 %
> 34 weeks	3	36	39	7.6 %

Table 1. Percentage of ROP in the Gestational Age Group

	< 32 Weeks	> 32 Weeks	P-Value
ROP +ve	47	7	< 0.0001 (chi square 56.016
ROP -ve	22	76	with 1-degree freedom)

Table 2. Association of Gestational Age with ROP

P value was calculated for gestational age <32 weeks and development of ROP using chi square test

Birthweight	With ROP	Without ROP	Total	% of ROP
< 1 Kg	5	2	7	71.4 %
1 – 1.3 Kg	31	18	49	63.2 %
1.31 - 1.5 Kg	10	29	39	25.6 %
1.51 - 1.8 Kg	7	38	45	15.5 %
> 1.8 Kg	1	11	12	8.3 %

Table 3. Percentage of ROP in Birth Weight Group

	< 1.5 Kg	> 1.5 Kg	P-Value
ROP +ve	46	8	<0.0001
ROP -Ve	49	49	

Table 4. Association of Birthweight with ROP

P value was calculated for birthweight < 1.5 Kg using Fishers two tail test

Sl. No.	Stage of ROP	No. of Cases (Total 54)	%
1	Stage I	24	44.4
2	Stage II	15	27.7
3	Stage III	10	18.5
4	Stage IV	3	5.5
5	Stage V	2	3.7

Table 5. Percentage of ROP in Various Stages

	Sex			P Value
	Male	Female		
Group ROP yes count	28	26	54	1.00
% within group	51.8 %	48.1 %	100 %	
ROP no count	52	46	98	
% within group	53 %	47 %	100 %	
Total count	80	72	152	
% within group	52.6 %	47.3 %	100 %	

Table 6. Association of Sex with ROP

There is no significant association between sex and ROP (P = 1.0)

	O2 Therapy		Total	P value
	Yes	No		
Group ROP yes count	32	22	54	0.0168
% within group	59.2 %	40.7 %	100 %	
ROP no count	37	61	98	
% within group	37.7 %	62.2 %	100 %	
Total count	69	83	152	
	45.4 %	54.6 %	100 %	

Table 7. Association of O_2 Therapy with ROP

DISCUSSION

Retinopathy of prematurity is a disorder of retinal vascular development in preterm infants. It continues to be a significant complication in preterm neonates despite advances in neonatal care and remains a major cause of childhood blindness worldwide.[8] The prevalence of ROP in this study was 35.5 % than that reported in many other studies; 24 %,[9] and 19.2 % in India.[10] The study conducted by Swarna Rekha et al.[11] also had same screening criteria which showed an incidence of ROP as 46 %.

In the Western studies the incidence rate of ROP was found to vary between 53 % - 88.5 % in babies with birth weight < 1000 g. In the present study the incidence was found to be 71.4 % which shows almost a similar pattern when compared to the previous studies. When the incidence of ROP in babies with birth weight < 1500g was noted to be 34.9 - 60.1 % in the Western studies, in the present study similar pattern was noted with incidence of 48.4 % in babies with birth weight < 1500 g.

Incidence of ROP was found to be nearly 80 % in babies with gestational age of < 28 weeks in many studies conducted previously. In the present study the incidence of ROP in babies with gestational age < 28 weeks was noted to be 66.6 % which was a bit lower than the previous studies. This may be due to a smaller number of babies in that age group and less survival rate. The incidence of ROP in babies with gestational age between 28 – 30 weeks group was noted to be nearly 27 % in the previous studies. In the present study the incidence of ROP in babies with gestational age between 28 - 30 weeks seems to be higher than the previous study which shows a rate of 76 %. This may be due to a greater number of babies in that age group.

As noted by many studies the most significant risk factors for the development of ROP was found to be low birth weight, low gestational age and prolonged oxygen therapy. In the present study, low-gestational age and low birth weight were found to be risk factors for development of ROP. As regard to the effect of low-gestational age on occurrence of ROP, in the present study we found it to be the most important risk factor in ROP. This shows similarity with the studies conducted by Shah et al.[12] Karna et al.[13] and Fortes et al.[14]

Many studies[12,14] found that low birth weight was associated with development of ROP. It was explained that in low birth weight babies there is need of prolonged oxygen therapy, ventilation, blood transfusion and chances of sepsis and all these also associated with development of ROP in low birth weight babies. In the present study we found that birth weight was significant factor for development of ROP, but relatively small number of patients (3 out of 152 cases) whose birth weight was less than 1000 g required oxygen therapy, prolonged ventilation, sepsis or blood transfusion.

Oxygen therapy was an independent risk factor for the development of ROP.[12] We found no statistically significant relationship between the occurrence of ROP and use of oxygen therapy. On the other hand, Palmer et al.[15] reported that oxygen therapy was a no significant factor for occurrence of ROP. They reported that ROP may develop in cases that did not receive oxygen therapy.

In present study 30 (55.5 %) babies required anti-VEGF out of whom 26 (86.66 %) achieved vascularisation with single dose treatment. These results are consistent with study done by Yang et al.[16]

CONCLUSIONS

In conclusion, the prevalence of ROP in the present study conducted at our institution was found to be 35.5 %. Based on the data interpretation of the present study the most important risk factors for the development of ROP were found out to be low gestational age and low birth weight. Clinicians importantly the neonatologists should have a

thorough knowledge of the other additional risk factors along with the known risk factors when monitoring preterm infants. As we all are aware of the fact that growth and development of medicine has achieved such a height so as to improve the survival of severe preterm infants. In severe preterm infants improved survival help us to analyse the new risk factors for the development of ROP.

Anti VEGF treatment is found to be more effective when compared to laser photocoagulation with less time taking for the treatment and simplicity of the procedure though not cost effective in our scenario. Screening of high-risk preterm infants is important and necessary to prevent the development, progression of ROP and also helps us for timely intervention and prevention of complications. As babies with low birth weight and older babies may also develop retinopathy of prematurity, it may be useful to extend screening for retinopathy of prematurity to babies with birth weight up to 1.8 Kg and older gestational age up to 36 weeks when exposed to risk factors like sepsis, apnoea, respiratory distress syndrome and those who need blood transfusion. If not detected at early stages as ROP may lead to complete loss of vision, more work has to be done in identifying risk factors and ROP markers to prevent development and progression of retinopathy of prematurity.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.
Financial or other competing interests: None.
Disclosure forms provided by the authors are available with the full text of this article at jebmh.com.

REFERENCES

[1] Coats DK, Aaron MM, Hussein MAW. Involution of retinopathy of prematurity after laser treatment: factors associated with development of retinal detachment. Am J Ophthalmol 2005;140(2):214-222.
[2] Dominico R, Davis DK, Coleman F, et al. Documenting the NICU design dilemma: comparative patient progress in open-ward and single family room units. J Perinatol 2011;31(4):281-288.
[3] Akçakaya AA, Yaylali SA, Erbil HH, et al. Screening for retinopathy of prematurity in a tertiary hospital in Istanbul: incidence and risk factors. J Pediatr Ophthalmol Strabismus 2012;49(1):21-25.
[4] Fanaroff AA, Martin RJ. Neonatal perinatal medicine. 7th edn. St. Louis: Mosby 2002: p. 676-745.
[5] Terry TL. Extreme prematurity and fibroblastic overgrowth of persistent vascular sheath behind each crystalline lens: I. Preliminary report. Am J Ophthalmol 1942;25:203-204.
[6] Tae-im K, Sohn J, Soo-Young P. Postnatal risk factors of retinopathy of prematurity. Paediatr Perinat Epidemiol 2004;18(2):130-134.
[7] International Committee for the Classification of Retinopathy of Prematurity. The International Classification of retinopathy of prematurity revisited. Arch Ophthalmol 2005;123(7):991-999.
[8] Section on Ophthalmology American Academy of Pediatrics, American Academy of Ophthalmology, American Association for Pediatric Ophthalmology and Strabismus. Screening examination of premature infants for retinopathy of prematurity. Pediatrics 2006;117(2):572-576.
[9] Murthy KR, Babu K, Benakappa N, et al. Analysis of risk factors for the development of ROP in preterm infants at a tertiary referral hospital in South India. Acta Medica Lituanica 2006;13(3):147-151.
[10] Hakeem AHAA, Mohamed GB, Othman MF. Retinopathy of prematurity: a study of prevalence and risk factors. Mid East Afr J Ophthalmol 2012;19(3):289-294.
[11] Rekha S, Battu RR. Retinopathy of prematurity: incidence and risk factors. Indian Pediatr 1996:33(12):999-1003.
[12] Shah VA, Yeo CL, Ling YLF, et al. Incidence, risk factors of retinopathy of prematurity among very low birth weight infants in Singapore. Ann Acad Med Singapore 2005;34(2):169-178.
[13] Gupta VP, Dhaliwal U, Sharma R, et al. Retinopathy of prematurity-risk factors. Indian J Pediatr 2004;71(10):887-892.
[14] Filho FJB, Eckert GU, Procianoy L, et al. 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 (Lond) 2009;23(1):25-30.
[15] Palmer AE, Hardy RJ, Dobson V, et al. 15-year outcomes following threshold retinopathy of prematurity: final results from the multicenter trial of cryotherapy for retinopathy of prematurity. Arch Ophthalmol 2005;123(3):311-318.
[16] Yang XM, Zhao YX, Wang ZH, et al. Effect of anti-VEGF treatment on retinopathy of prematurity in Zone II Stage 3+. Int J Ophthalmol 2018;11(4):641-644.