

# A STUDY ON EFFICACY OF LASER PHOTOCOAGULATION IN THE MANAGEMENT OF RETINOPATHY OF PREMATURITY AMONG NEONATES

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## ABSTRACT

**Background:** Retinopathy of Prematurity (ROP), is a disease process seen in preterm low birth weight infants that affects the normal retinal vascular development. In case of a premature birth the process of normal retinal vascular development is altered and abnormal neovascularization ensues, thus making this disease one of the major emerging causes of childhood blindness accounting for 38 to 47% of childhood blindness in India. Management of Retinopathy of Prematurity differs in modalities depending on the Stage and extent of the disease. Laser Photocoagulation is the treatment of choice and the most common modality advocated for early management to provide better prognosis. **Aim:** This study evaluated the clinical outcome and efficacy of laser photocoagulation in the management of retinopathy of prematurity among neonates at a tertiary Care hospital in Hyderabad. **Materials and Methods:** This is a prospective interventional study conducted at a tertiary eye care Hospital during December 2019 to June 2021 with a sample size of 30 from the Neonates screened for ROP at Sarojini Devi Eye Hospital and Niloufer Children's Hospital, Hyderabad. In this small study, all the neonates with birth weight less than 1500 gms and age of gestation less than 32 weeks with the help of a Binocular Indirect Ophthalmoscope and diagnosed with Threshold for treatment ROP were treated by Laser photocoagulation using the Laser Indirect Ophthalmoscope delivery system. **Result:** All neonates treated were followed up for outcome. 30 neonates underwent confluent laser

photocoagulation at a mean postconceptional age of 36.4 weeks (range 32-40 weeks). The mean post-laser follow-up visits were 5 (range 4-8) i.e. upto postconceptional age of 46.25 weeks (range 40-53). It was observed that Laser had a favourable outcome in 25 patients (83.3%) who showed regression of the disease. 5 patients (16.7%) showed progression even after 2 treatment sessions and they were planned for Intravitreal anti-VEGF later. **Conclusion:** Thus, it can be concluded that effective screening strategies especially in at risk babies (pre-term and/or Low birth weight) leading to early diagnosis of ROP and timely treatment help in preserving vision and preventing blindness in neonates.

**Keywords:** Retinopathy of prematurity, Laser photocoagulation.

### **Introduction:**

Retinopathy of Prematurity (ROP), initially named as Retrolental Fibroplasia by Terry in 1942, is a disease process that affects the normal retinal vascular development in premature infants. It is one of the major causes for preventable blindness in children across both the developed and developing countries. The rapid increase in the number of Neonatal intensive care units and improved access to these NICUs has increased the survival rates of premature infants in developing countries like India, thereby, resulting in rise of ROP incidence.

It is estimated that globally ROP affects more than 50,000 infants annually and in India, every year, around 500 children become blind from ROP.<sup>1</sup> Currently, the incidence of ROP reported in India is 38% to 47%.<sup>2,3,4</sup>

Retinopathy of prematurity has a wide spectrum ranging from mild transient changes in retina with regression to severe progressive vasoproliferation, scarring, retinal detachment and blindness. However, it has a good prognosis if identified early and managed appropriately.

In 1942, Terry first described the implication of oxygen therapy as the causative agent for retrolental fibroplasia.<sup>5</sup> Today, the huge number of studies on ROP have revealed that oxygen administration is not the only causative factor, but many other risk factors play a role in the pathogenesis of ROP.<sup>6</sup>

There are various modalities for the management of retinopathy of prematurity depending on the stage and extent of the disease such as cryotherapy, laser photocoagulation is the treatment of choice and mostly advocated for early management, intravitreal anti VEGF injections and surgeries like scleral buckling and vitrectomy are done when the disease progresses to stage 4 or beyond resulting in retinal detachment.

The natural history of the disease is spontaneous resolution, that is it may stop progressing and/or revert to re-establish the normal vascular development. If the disease progresses it may lead to unfavourable sequelae like: Retinal Detachment, Retinal folds and Macular dragging causing pseudostrabismus, strabismus, microphthalmos, amblyopia as a result of myopia, cataract, glaucoma and pthisis bulbi.

Hence, this brings us to ethically and professionally justifiable reasons regarding the requirement for our study. With early diagnosis and effective treatment there is a potential for achievement of normal vision and prevention of blindness in every infant with this disease. This study evaluated the clinical outcome and efficacy of laser photocoagulation in the management of retinopathy of prematurity among neonates at a tertiary Care hospital in Hyderabad.

### **Materials and Methods:**

This is a prospective interventional study conducted at a tertiary eye care Hospital during December 2019 to June 2021 with a sample size of 30 from the Neonates screened for ROP at Sarojini Devi Eye Hospital and Niloufer Children's Hospital, Hyderabad. Infants diagnosed with retinopathy of prematurity during screening and require laser therapy according to ETROP guidelines were included in the study. Infants diagnosed with retinopathy of prematurity but do not require laser therapy, stages of IV and V of ROP and cases with vitreous haemorrhage were excluded from the study. Informed consent of parents was taken after explaining in detail about the methods and procedures involved in the study in their own vernacular language. Whenever the neonate was advised for Laser Photocoagulation a separate consent was obtained from the parents explaining about the procedure and its possible merits and de-merits. Ethical clearance was obtained from the institution. Screening was done at 4 weeks postnatally for infants with birth weight :- <1500gms and 1501-2000gms with significant risk factors Gestational age of less than 32 weeks and 32-36 weeks with significant risk factors. Pupils of both eyes were dilated with 0.8% tropicamide and 2.5% phenylephrine hydrochloride, 1 drop instilled into each eye 3 times 10 minutes apart. 0.5% proparacaine was used as topical anaesthetic. Anterior segment examination was done to rule out hazy cornea, rigid pupil and leukocoria. Fundus evaluation with +20 D lens and a binocular indirect ophthalmoscope was done and a sterilized paediatric speculum and scleral indenters were used to view the retinal periphery. From the infants screened those satisfying the inclusion and exclusion criteria were registered. The findings were recorded with diagrams and plan of management according to

the Revised ICROP classification 2005 and ETROP. A card was given to the parents which bore the diagnosis and schedule for further follow-up. Treatment guidelines based on ETROP (Early Treatment of ROP) clinical trial were as follows; Type 1 includes treatment is recommended within 72 hours. It includes any ROP stage in zone I when accompanied by plus disease, stage 3 to any extent in zone I, without plus disease, stage 2 or 3 in zone II, with plus disease and stage 3 in zone III, without plus disease. Type 2 requires observation and follow up. It includes stage 1 or 2 in zone I without plus disease and stage 3 within zone II without plus disease. Prior to the procedure a consent was obtained from the parents after giving a detailed explanation about the merits and possible complications of the laser procedure in their own vernacular language.

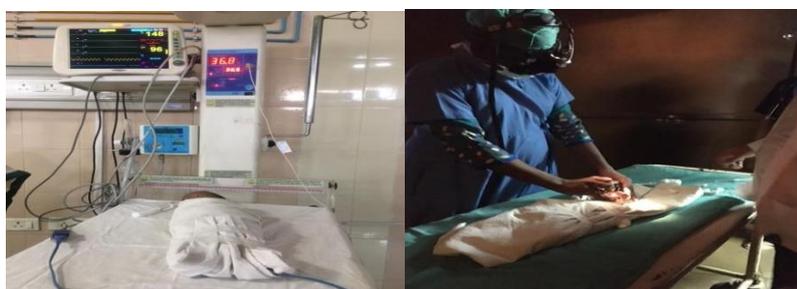


Figure 1: Procedure of LIO

The mother of the infant was asked to feed and burp the baby 30 – 60 minutes before treatment. The pupils of affected eyes were dilated with 0.8% tropicamide and 2.5% Phenylephrine hydrochloride around half an hour before the procedure. 0.5% paracaine was applied topically to anaesthetize the eye. The infants were monitored with a pulse oximeter by a neonatologist. Heart rate and apnoea spells also were monitored. Photocoagulation of peripheral retina was done using a 532 nm diode laser by an indirect ophthalmoscope system. Laser burns less than half burn width apart known as Confluent burns were applied. The number of laser applications given were according to the size of the avascular zone in the eye. Antibiotic and anti-inflammatory eye drops were given 4 times a day for 1 week following laser. Any complications during and after laser treatment were noted. Post treatment outcome was retrieved and analysed. All the treatment details were duly filled in the patient's card and proforma and parents were informed as to the next follow-up visit.

Follow up examination was done as follows for Zone 2 and beyond – at 5 or 7 days post-laser and for Zone 1 or APROP or eyes with hazy media – at 3-4 days and laser was redone if needed. Retinal images were obtained using the wide-angle fundus camera called Retcam before and after laser therapy and at subsequent follow ups. The frequencies method gives statistics and graphical presentations that are helpful for depicting many sorts

of variables. The crosstabs procedure forms two-way and multiway tables and provides a variety of tests and measures of association for two-way tables. The structure of the table and whether categories are ordered determine what test or measure to use. The Chi-Square Test procedure tabulates a variable into categories and computes a chi-square statistic. This goodness-of-fit test compares the observed and expected frequencies in each category to test either that all categories contain the same proportion of values or that each category contains a user-specified proportion of values.

**Results:** Considering the inclusion and exclusion criteria, a total of 30 neonates (60 eyes) treated with laser photocoagulation were followed up over the 18 months of study.

Table 1: Distribution based on stages and zones of ROP.

<b>Stages of ROP</b>	<b>Frequency</b>	<b>Percentage</b>
Stage 1	3	10
Stage 2	16	53.3
Stage 3 (incl. APROP)	11	36.7
Total	30	100
<b>Zones of ROP</b>	<b>Frequency</b>	<b>Percentage</b>
Zone 1	3	10
Zone 2	25	83.3
Zone 3	2	6.7
Total	30	100

Table 1 shows that out of the 30 neonates lasered, 3 (10%) had Stage 1, 16 (53.3%) had Stage 2, 11 (36.7%) had Stage 3 (including APROP). It was observed that 3 neonates (10%) had involvement of zone 1, 25 (83.3%) had involvement of zone 2 and 2 (6.7%) had involvement of zone 3.

Table 2: Distribution based on gender, birth weight (gms), gestational age.

<b>Gender</b>	<b>Frequency</b>	<b>Percentage</b>
Male	15	50
Female	15	50
Total	30	100
<b>Birth Weight (gms)</b>	<b>Frequency</b>	<b>Percentage</b>
<1500g	24	80
>1500g with risk factors	6	20
Total	30	100

<b>Gestational Age (weeks)</b>	<b>Frequency</b>	<b>Percentage</b>
Less than 32 weeks	25	83.3
32-36 weeks with risk factor	5	16.7
Total	30	100

Table 2 shows among the 30 neonates that underwent laser photocoagulation, 15 (50%) were males and 15 (50%) were females, 24 (80%) had Birth weight less than 1500g and 6 (20%) had birth weight more than 1500g. 25 neonates (83.3%) were born at less than 32 weeks and 5 (16.7%) had gestational age above 32 weeks.

Table 3: Distribution based on laser sittings,

<b>Laser Sittings (weeks)</b>	<b>Frequency</b>	<b>Percentage</b>
One	18	60
Two	10	33.3
Three	2	6.7
Total	30	100
<b>Post laser follow up visits</b>	<b>Frequency</b>	<b>Percentage</b>
Four	8	26.7
Five	18	60
Seven	3	10
Eight	1	3.3
Total	30	100

All 30 babies (60 eyes) underwent confluent laser photocoagulation at a mean post-conceptual age of 36.4 weeks (range 32-40 weeks). Out of the 30 neonates, 2 (6.7%) needed 3 laser sittings, 10 (33.3%) needed 2 laser sessions and remaining 18 (60%) needed 1 laser sitting. Post-laser all the patients were followed up until there was complete regression of the disease. The mean post-laser follow-up visits were 5 (range 4-8) i.e. upto postconceptional age of 46.25 weeks (range 40-53). All the parents were compliant and did not miss any visit for follow-up. It was observed that Laser had a favourable outcome in 25 patients (83.3%) who showed regression of the disease. 5 patients (16.7%) showed progression even after 2 treatment sessions and they were planned for intravitreal anti VEGF later.

Table 4: Follow up visits

Follow up visits (weeks)	Frequency	Percentage
Two	6	20
Three	8	26.7
Four	16	53.3
Total	30	100

Table 4 shows that 6 (20%) patients came for two weeks, 8 (26.7%) patients came for four weeks, 16 (53.3%) came for four weeks follow up. All were valid.

Table 5: ROP regressed Y/N

ROP regressed Y/N	Frequency	Percentage
Yes	25	83.3
No	5	16.7
Total	30	100

Table 5 shows that 25 patients (83.3%) were ROP regressed.

Table 6: Statistics

Parameters	Birth weight (g)	Gestational age (wks)	Follow up visits	Laser sittings	Post laser follow up
Valid	30	30	30	30	30
Missing	0	0	0	0	0
Mean	1203.83	28.93	3.33	1.47	5.03
Median	1140.00	28.00	4.00	1.00	5.00
Mode	1000	28	4	1	5
Std deviation	228.348	1.856	0.802	0.629	0.999
Variance	52142.971	3.444	0.644	0.395	0.999
Range	850	6	2	2	4
Minimum	900	26	2	1	4
Maximum	1750	32	4	3	8

Table 7: Crosstabs: Birth weight (gm) group\*ROP regressed Y/N.

Birth weight (g) group	ROP regressed Y/N			Total
		Yes	No	
	<1500g	Count	19	5
	Percentage	79.2%	20.8%	100%

	>1500g with risk factors	Count	6	0	6
		Percentage	100%	0	100%
	Total	Count	25	5	30
		Percentage	83.3%	16.7%	100%

Chi square tests value was 1.5, df was 1, asymptomatic significance (2 sided) was 0.221.

Table 8: Crosstabs: Gestational age group (weeks)\*ROP regressed Y/N.

		ROP regressed Y/N			Total
			Yes	No	
<b>Gestational Age (weeks) group</b>	<32 weeks	Count	20	5	25
		Percentage	80%	20%	100%
	32-36 weeks with risk factor	Count	5	0	5
		Percentage	100%	0	100%
	Total	Count	25	5	30
		Percentage	83.3%	16.7%	100%

Chi square tests value was 1.2, df was 1, asymptomatic significance (2 sided) was 0.221.

It was observed that, all the cases in which ROP did not regress, had birth weight of less than 1500 gm and gestational age of less than 32 weeks. However, this association proved insignificant in this study. Therefore, more number of studies are required to analyze this association.

**Discussion:** ROP has turned into a significant challenge for India. With further developing advances in neonatal care, the survival rates of low and very low birth weight babies have expanded and this has prompted a striking expansion in the occurrence of ROP which is expected to increase further in the near future.

Legitimate working of the framework for screening of neonates in different hospitals across the nation will assist in diagnosing the illness at the soonest and with appropriate therapy the lives of numerous children will be saved from the adverse impacts of this disease.

It is important for ophthalmologists to become familiar with the appearance of normal retina in new-born children to analyse ROP effectively among the diverse fundoscopic pictures that one goes over while screening the babies. The utilization of a

binocular indirect ophthalmoscope is essential for adequate assessment. Scleral indenters can be utilized occasionally to visualize the periphery.<sup>7</sup>

With the advent of indirect ophthalmoscopic delivery system, laser photocoagulation has become progressively the best option of treatment because of its few adverse effects and many benefits. It deters the requirement for general sedation, it is related with altogether less morbidity and there is no external reaction like conjunctival chemosis. The utilization of infant scleral depressor has allowed us to treat right upto the ora serrata with indirect laser photocoagulation.<sup>8</sup>

The Diode laser enjoys an upper hand over Argon laser photocoagulation wherein the main trouble is the presence of tunica vasculosa lentis. Hittner et al. (quoted by Isenberg<sup>9</sup>) have described and graded the anterior vascular capsule (tunica vasculosa lentis) and shown it to correlate well with the gestational age. Hence, significant remnants of the same can be expected in some of those infants born premature. The haemoglobin in the blood column of the blood vessels can absorb argon laser energy and due to their proximity to the anterior lens capsule could lead to lenticular burns. Several studies reported the outcome of posterior ROP after laser therapy. Different studies used different criteria therefore it is difficult to compare them. In earlier studies, Capone et al<sup>10</sup> reported a 17% unfavourable outcome in Zone 1 ROP treated with a diode laser at the threshold stage. The possible benefits of early treatment for posterior ROP treated with a laser were discussed in a subsequent study by Vander et al<sup>11</sup> and Shah et al<sup>12</sup> reported an 82% rate of favourable outcome in their series of fulminate ROP treated with confluent laser photocoagulation. Katz et al<sup>13</sup> reported a 40% unfavourable outcome for Zone 1 cases, but in this study, there was a mixture of cases treated at varying stages of the disease, some of them having passed even the threshold stage. Kychenthal et al<sup>14</sup> reported a favourable result in 54.4% of eyes with Zone 1 disease treated with laser photocoagulation. (56,57,58,59,60). Sudha Chaudhari et al<sup>15</sup> conducted a prospective study at KEM Hospital Pune to analyse the outcomes of laser photocoagulation in ROP. Out of 552 infants that were screened 123 had ROP and Laser photocoagulation was done in 41 infants. All babies withstood the procedure well and there were no post-laser complications other than reddening of the conjunctiva, which disappeared in 2-3 days. The results of laser were extremely satisfactory and only 2 children (9%) had poor outcome, out of the 22 children who were available for 3 year follow up. T.Tsitsis et al<sup>16</sup> conducted a study to determine the effectiveness of laser photocoagulation in eyes with threshold retinopathy of prematurity (ROP) in Philadelphia USA. During the 41-60

months follow-up 27 of 31 lasered eyes (87%) demonstrated regression of the extraretinal neovascularization, and 26 (84%) had functional vision. Thus follow-up of patients treated with diode laser demonstrates that functional vision is attainable. David G Hunter and Michael X Repka<sup>17</sup> compared laser photocoagulation with cryotherapy at Johns Hopkins University Baltimore. The diode laser treatment was better tolerated than cryotherapy, and the treatment apparatus was more easily transported. Apnoeic episodes requiring intubation resulted from two cryotherapy sessions but no diode laser sessions. Five cryotherapy-treated eyes required retreatment because of persistent disease with adjacent skip areas. Malathi V.K, Ramya Chelliah and KR.Sowmiya<sup>18</sup> analysed the outcome of laser photocoagulation in management of ROP at Tagore Medical College and Hospital, Chennai. Out of the 202 babies screened, 73(36.14%) babies had ROP among which 17 (23.28%) required laser treatment. 14 (82.35%) babies treated with laser recovered while 3(17.64%) progressed to severe disease. This included two babies who did not respond to even a second sitting of laser and one baby who was brought late for review and developed retinal detachment. From the study it was found that Pre-threshold and threshold ROP responded very well to laser treatment and that the 532nm had a good outcome and efficacy comparable to diode laser. All the diagnosed infants were treated immediately and followed an aggressive approach with confluent laser photocoagulation. This has proved to be a significant factor for a high success rate and also accounts for the lesser number of mean treatments in the present study.

**Conclusion:** It can be concluded that with effective screening strategies for early diagnosis of affected neonates, followed by, adequate treatment with Laser, complete resolution of the condition and prevention of its progression can be achieved. Each and every infant if diagnosed on time and effectively treated has the potential to achieve normal vision throughout life.

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