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Correlation of retinopathy of prematurity with oxygen saturation in preterm babies in a tertiary care center: A noble guide

Shahjadi Praveen¹, Syed Manazir Ali², Naheed Akhtar¹, Waris Abdul¹,
Rajendra P Maurya^{3*}¹Dept. of Ophthalmology, Institute of Ophthalmology, JNMCH, Aligarh Muslim University, Aligarh, Uttar Pradesh, India²Dept. of Paediatrics, JNMCH, Aligarh Muslim University, Aligarh, Uttar Pradesh, India³Regional Institute of Ophthalmology, IMS, Banaras Hindu University, Varanasi, Uttar Pradesh, India

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ABSTRACT

Objective: To find the correlation of retinopathy of prematurity (ROP) with oxygen saturation among preterm babies in neonatal intensive care unit (NICU) of a tertiary care centre.**Material and Methods:** This Prospective cross-sectional study was conducted on 64 premature neonates of gestational age < 36 weeks who were on oxygen and were admitted in NICU after obtaining ethical clearance. We compare the effect of two oxygenation strategies on development of ROP in two groups. Oxygen ranged from 86-90% in one group (32 neonates) and 91-94% in another group (32 neonates). Screening of all neonates were done by one examiner.**Statistical Analysis:** The data were analyzed using Statistical Package for the Social Sciences (SPSS) version 26. For categorical data, Chi-square test was used. For continuous data, Mann Whitney U test were used and p-value < 0.05 was taken as significant.**Results:** Among 64 babies, 32 babies were on 86-90% of oxygen, 5 babies had disease and the remaining 32 babies who were on 91-94% of oxygen, 14 babies had developed disease showed a statistically significant relationship between ROP and oxygen saturation (p=0.014).**Conclusions:** High oxygen saturation target is one of the important risk factors leading to the development of ROP. Lower oxygen saturation reduced the prevalence as well as had no deleterious effect on general health of baby. Therefore, accurate measurement of oxygen concentration by probe and proper monitoring of SpO2 levels must be done in every NICU.This is an Open Access (OA) journal, and articles are distributed under the terms of the [Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License](https://creativecommons.org/licenses/by-nc-sa/4.0/), which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.For reprints contact: reprint@ipinnovative.com

1. Introduction

Retinopathy of prematurity [ROP] is a retinal neo-vascular disorder that can, in its most severe state, lead to severe vision loss.¹ It is characterized by abnormal development of retinal vasculature in preterm babies and is an important and preventable cause of childhood blindness.²⁻⁴ In a young country like India ROP can be catastrophic, hence it is important to catch the bull by the horn at the earliest.

The term Retinopathy of prematurity was first explained by Terry in 1942 and is now recognized as an emerging cause of childhood blindness worldwide.⁴ Risk factors of ROP appears to be multifactorial and complex which includes gestational age <32 weeks, low birth weight <1500 grams, supplemental oxygen, respiratory distress syndrome, shock, sepsis, hypoxia, anaemia, blood transfusion and genetic factors.⁵ As we know that prolonged use of higher supplemental oxygen is the most frequently identified risk factor for severe ROP requiring treatment. Flynn et al.⁶ in 1992 found that the time duration at which transcutaneous

* Corresponding author.

E-mail address: mauryarp_bhu@yahoo.com (R. P. Maurya).

PO₂ \geq 80 mmHg showed a significant association with incidence and severity of ROP. Despite several studies done previously, the ideal range of oxygen saturation target remains controversial. Many of the risk factors arise in the NICU itself and some of them are avoidable. So, cautious monitoring of the risk factors is necessary to reduce the burden of disease. Recent estimate show that there are at least 1.26 million children who are blind from ROP globally, out of which 280000 children are from India.^{7,8} Now the incidence and burden of disease has been increasing with time due to increased survival of preterm babies, better quality of neonatal care and low coverage of screening and treatment for ROP. The clinical domain of ROP extends from spontaneous regression of disease to total retinal detachment leading to complete blindness. The final outcome of end stage disease and its treatment modality is not very good. Hence, screening guidelines for early detection of disease and intervention at the earliest if needed can be done to decrease the incidence and burden of disease. Babies having significant ROP have increased risk of refractive error (high myopia), strabismus, amblyopia, glaucoma and retinal detachment.

2. Materials and Methods

This was a prospective cross-sectional study conducted among 64 preterm infants from November 2019 to October 2021 after obtaining ethical clearance from the institutional Ethical Committee and was according to the Declaration of Helsinki guidelines. An informed written consent was signed by each patient's attendant before examination. Preterm infants of gestational age less than 36 weeks, who was on oxygen supplementation and were admitted in Neonatal Intensive Care Unit of a tertiary care centre were enrolled in our study.

We compare the effect of two oxygenation strategies on the development and severity of Retinopathy of Prematurity in two groups of infants. One group (32 infants) have received oxygen between 86-90% and another group (32 infants) have received oxygen between 91-94%. A brief clinical history was taken followed by dilatation of pupil with mydriatic eye drop after instilling every 15 minutes for 3-4 times. Paracaine eye drop was instilled and Alfonso eye speculum was inserted and anterior segment examination was done by direct Ophthalmoscope. Peripheral and central retinal examination was done by binocular indirect ophthalmoscope and scleral depressor was used to indent the eye and finding were noted on a predesigned proforma. Staging was done according to international classification of retinopathy of prematurity (ICROP) and patient with avascular temporal peripheral retina were asked to review in retina clinic or NICU until retinal vascularization reaches zone III. All infants enrolled in our study were screened between third to fourth weeks of life after birth except for infants with gestational age less than or equal to 28 weeks

or birth weight less than 1200 grams. Such infants were screened between second to third weeks of gestational age.

3. Results

Among 64 babies gestational age ranged from 196 to 252 days with mean gestational age of 229.25 ± 14.73 days and birth weight ranged from 660 to 2280 grams with a mean birth weight of 1554.21 ± 367.92 grams described in (Table 1)

Among 64 babies, 32 babies were on 86-90% of oxygen, 5 babies had developed ROP and remaining 32 babies were on 91-94% of oxygen, 14 babies had developed ROP. A statistically significant relationship was observed ($p=0.014$) described in (Table 2).

The mean duration of oxygen exposure was 16.78 ± 7.85 days in babies who had ROP and was 9.22 ± 5.89 days in babies who did not developed ROP. A statistically significant relationship was seen ($p=0.000$) described in (Table 3).

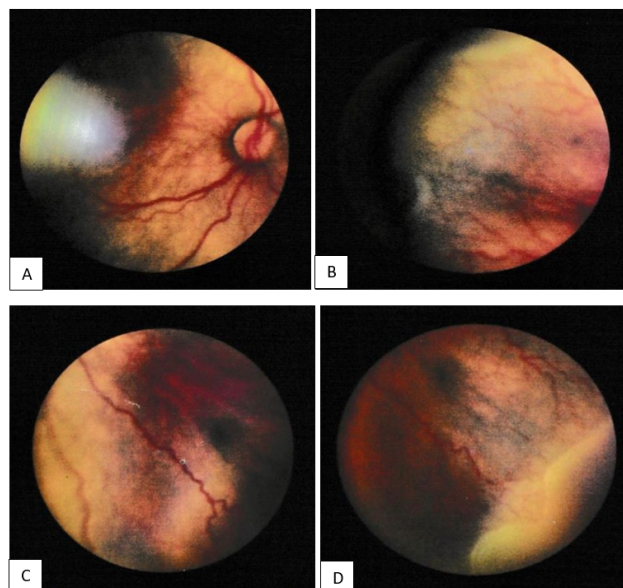


Figure 1: A): Central fundus showing mild vascular tortuosity; B): Stage 2, Zone 2 anterior; C): ROP stage 3, Zone 2 with plus disease; D): Tortuosity of vessels in plus disease

4. Discussion

ROP is an important and preventable cause of childhood blindness if screened, diagnosed and treated at the earliest. Middle income countries including India is currently facing the third epidemic of the ROP and blindness related to it. This makes screening an important factor in decreasing ROP related blindness. If oxygen saturation is increased it saves the life of premature babies but does increase the risk of ROP, hence an optimum oxygen saturation which balances

Table 1: Demographic data of the enrolled babies

	N	Minimum	Maximum	Mean	SD
Gestational age (days)	64	196	252	229.25	14.73
Birth weight (grams)	64	660	2280	1554.21	367.92

Table 2: Association between oxygen saturation given at birth and ROP

	Range	ROP		Total	χ^2	df	p- value
		Present	Absent				
Oxygen saturation	86-90%	5	27	32	6.063	1	0.014
	91-94%	14	18	32			

Table 3: Association between duration of oxygen given and ROP

	ROP	N	Mean(days)	SD	df	p- value
Duration of oxygen given (days)	Present	19	16.78	7.85	62	0.000
	Absent	45	9.22	5.89		

ROP risks and saves life of these babies is mandatory. This necessitates the acquisition of proper records of data about the babies at risk and appropriate guideline to tackle this disease. This study was conducted in neonatal intensive care unit of a tertiary care centre in collaboration with department of Ophthalmology.

The study group comprises of 64 premature babies out of which 38(59.4%) were male and 26(40.6%) were female. Mean birth weight of babies were 1447.18 ± 288.38 grams (range: 660-2280 grams) and mean gestational age of babies were 223.27 ± 16.25 days (range: 190-252 days) (Table 1). Out of 64 babies, 18 (28.12%) were delivered normally and 46 (71.87%) were delivered by caesarean section.

In our study, we compared the target ranges of oxygen saturation of 86% to 90% versus 91% to 94% among 64 infants and found that ROP occurred less frequently in babies who was on lower oxygen saturation target. We observed a significant relationship between oxygen supplementation and development of ROP (p value-0.014) (Table 2). Our study was supported by Benefits of Oxygen Saturation Targeting Study II (BOOST –II)⁹ conducted in United Kingdom and Australia and found that babies at lower oxygen saturation target showed low incidence of ROP but mortality was high. Hartnett ME et al.¹⁰ in 2013 conducted a study in which they compared target ranges of oxygen saturation of 85% to 89% versus 91% to 95% and concluded that severe retinopathy occurred less frequently in survivors of the 85% to 89% saturation group. Wright et al.¹¹ in 2006 found that by maintaining SpO₂ target between 83% to 93% in the immediate post gestational life in combination with strict oxygen fluctuation control prevents further development of severe ROP. Tlucek PS et al.¹² concluded that lowering oxygen saturation target was associated with decreased incidence of ROP in infants with weight less than 1000 grams and Gantz MG et al.¹³ in 2020 found that significant association was present between duration of oxygen given and time

in particular achieved saturation ranges. They concluded that Infants who spent longer time at higher range of SpO₂ was associated with increased odds of severe ROP. All of them reported a statistically significant relationship between range of oxygen saturation and development of ROP. As we know that in our study, oxygen saturation was measured by pulse oximeter and it does not give exact estimation of oxygen concentration. We could find accurate measurement of oxygen concentration and its fluctuation by means of probe which gives us precise information about oxygen saturation and further implementation of controlled supplemental oxygen therapy in preterm babies.

In our study, we also compared the effect of duration of oxygen supplementation and development of ROP and we observed a significant relationship with p value of 0.000 (Table 3). Results was also supported by Ashton N et al.¹⁴ found that severity of vaso obliterative effect of oxygen is directly proportional to duration of oxygen administered and its concentration and Ugrubas SC et al.¹⁵ found significant relationship among the factors like gestational age, total duration of oxygen supplementation and birth weight. All of them found a significant relationship between ROP and duration of oxygen supplementation. Therefore, Neonatologist should try to wean off supplemental oxygen as early as possible.

5. Limitation of study

As we know that pulse oximeter was used for oxygen saturation measurement in our study. We could find accurate measurement of oxygen concentration and its fluctuation by means of oxygen probe which gives us precise information about oxygen saturation and further implementation of controlled supplemental oxygen therapy in preterm babies.

6. Conclusion

ROP is a vision threatening disease mainly affecting premature neonates. From our study, we know that higher supplemental oxygen therapy was found as one of the most important risk factors leading to development of ROP. Hence, an optimum oxygen saturation range which balances ROP risks and saves life of babies is mandatory. Mostly in NICU oxygen is measured with pulse oximetry which does not give accurate estimation of oxygen concentration. We could use oxygen probe for precise information about fluctuation and concentration of oxygen given to babies. We feel that a large-scale community-based study rather than a single hospital-based study with long term follow-up is warranted to confirm the outcomes of lower oxygen saturation in terms of morbidity and mortality.

6.1. Carry home message

1. High supplemental oxygen therapy for longer duration was found to be an important risk factor leading to development of ROP. Therefore, accurate measurement of oxygen concentration by oxygen probe and proper monitoring of SpO₂ level must be done in every NICU.
2. Neonatologist should try to wean off supplemental oxygen as early as possible.
3. Every high-risk baby admitted in NICU must undergo ophthalmological examination at the end of first month of life. If not possible, screening should be done prior to discharge of baby.
4. Proper record of all babies including birth weight, gestational age, history of oxygen supplementation, number of days of therapy, other co morbidities, contact number of parents, complete staging of ROP and further follow up date should be mentioned in files and communicated to parents.
5. Adequate number of trained Vitro-retinal surgeon is required for screening and treatment of ROP as middle-income countries like India is currently facing the third epidemic of ROP.
6. Teleconsultation and outreach programs should be conducted by trained specialist in medical retina.
7. The family can be counselled about low vision aid and the future prospect of bionic eye.
8. Many governments associated programme in this field are required to increase the awareness among parents about the disease and its consequence if not treated at time.

7. Source of Funding

The authors received no funding for this study.

8. Conflict of Interest

The authors declare that they have no conflict of interest.

9. Ethical Approval

Ethical clearance was obtained from Institutional Ethical committee of Jawaharlal Nehru Medical College and Hospital, A.M.U., Aligarh.

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Author biography

Shahjadi Praveen, Junior Resident

Syed Manazir Ali, Professor

Naheed Akhtar, Assistant Professor  <https://orcid.org/0000-0003-0282-2342>

Waris Abdul, Professor  <https://orcid.org/0000-0002-3210-7633>

Rajendra P Maurya, Associate Professor  <https://orcid.org/0000-0001-9343-6003>

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