



# Correlation of Retinopathy of Prematurity with Oxygen Saturation

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## Abstract

Retinopathy of prematurity (ROP) is an abnormal vascular proliferative disease of retina that affects preterm infants. It is a leading cause of childhood blindness worldwide despite improvement in neonatal care and management. Earlier ROP was found to be associated with oxygen therapy only. Now it was concluded that aetiology of ROP was multifactorial but three factors have shown significant association with ROP: low gestational age (GA), low birth weight (BW), prolonged exposure to supplementary oxygen following delivery. Several investigators reported that lower oxygen saturation targets at young post-gestational ages with increased oxygen saturation targets at older post gestational ages reduced the incidence of ROP. However previous clinical studies are not conclusive.

**Keywords:** Retinopathy of Prematurity, Oxygen saturation, Gestational age, Birth weight

## Introduction

Retinopathy of prematurity [ROP] is a retinal neo-vascular disorder that can lead to severe vision loss [1]. It is mainly characterized by abnormal development of retinal vasculature. It is an important and preventable cause of childhood blindness [2]. Retinopathy of prematurity [ROP] is now recognized as a important cause of childhood blindness worldwide [3]. The causative factors of ROP is multifactorial and complex. It includes prematurity with a gestational age <32weeks and low birth weight [LBW] <1500 gram. Other risk factors, includes anaemia needing blood transfusion, prolonged exposure to supplementary oxygen, sepsis, apnea, comorbidities of prematurity, nutrition, and genetic factors [4].

ROP is an important cause of childhood blindness in countries, such as United States, and is also emerging as a major cause of blindness [the third epidemic]; in middle income countries [5]. In India, proportion of severe visual impairment and blindness due to ROP in children aged 0-15 years in school for the blind is 0.2% [6].

## Pathogenesis

The growth of retinal vessels is guided mainly by an endothelial-cell specific mitogen which is vascular endothelial growth factor [VEGF], is one of the key angiogenic molecules implicated in pathogenesis. It consists of two phases:-

**Phase 1:** Hyperoxia → Downregulation of VEGF → Vessel migration halt

**Phase 2:** Hypoxia → VEGF production → Neovascularization and fibrous proliferation.

However, by maintaining SpO<sub>2</sub> values between 83% to 93% in immediate post gestation life, combined with strict oxygen fluctuations, it is possible to prevent the early vaso-obliterative phase and subsequent development of severe ROP.

## Relation between Oxygen Saturation and Retinopathy of Prematurity

Many studies have been performed across the world to determine the effect of oxygen saturation on retinopathy of prematurity. **McGregor ML et al. in 2002** [7] conducted a prospective study in which a total of 229 STOP-ROP infants were compared with 136 HOPE-ROP infants enrolled during the same time period from same 15 hospital showed that HOPE-ROP infants progressed from pre-threshold to threshold ROP less often than STOP-ROP infants. It seems that SpO<sub>2</sub> value at the time of pre-threshold diagnosis is a prognostic indicator for which infants may progress to severe ROP. **York et al. in 2004** [8] provided strong evidence that fluctuations in oxygen saturation target at several time duration upto 30 days following birth increased the odds of a preterm infant developing severe ROP. **Vanderveen DK et al. in 2006** [9] conducted a study in which he concluded that change in oximeter alarm parameters in

the first weeks of life for infant with weight <1250g may decrease the incidence of prethreshold ROP. **Sears JE, et al. in 2009** <sup>[10]</sup> conducted a prospective study in which he concluded that higher oxygen target at older gestational age and lower oxygen target at early gestational age decreased the severity and incidence of ROP. **Chen ML et al. in 2010** <sup>[11]</sup> conducted a study among preterm infants with a gestational age of < 32 weeks, found that early low and late high oxygen saturation were associated with a reduced risk of severe ROP. **Hartnett ME et al. in 2013** <sup>[12]</sup> conducted a randomized multicenter study, Surfactant, Positive Airway Pressure, Pulse Oximetry Randomized Trial [SUPPORT] from the neonatal research network. They concluded that severe retinopathy occurred less frequently in survivors of the 85% to 89% saturation group [Relative Risk: 0.52 (95% CI, 0.37-0.73; p<0.001)]. **Alizadeh et al. in 2015** <sup>[13]</sup> did a cross-sectional retrospective study at Amir-al-momenin Eye Hospital, Iran concluded that oxygen therapy was not an independent risk factor for development of ROP. **Le et al. in 2016** <sup>[14]</sup> found the incidence of ROP in their study conducted at NICU of a tertiary care hospital located in Hyderabad as 2.3%.

## Conclusion

Retinopathy of prematurity is a preventable eye disorder. Studies have shown that lower oxygen saturation target in early postnatal weeks and high oxygen saturation target at PMA of more than or equal to 32 weeks was associated with a decreased risk of ROP. Using a pulse oximeter and blender to provide the required oxygen dose for that target are simple and effective approaches in reducing ROP risk. We feel that a large randomized clinical trial with long term developmental follow up is required to determine the effect of oxygen saturation in ROP.

## List of abbreviations

Retinopathy of prematurity (ROP)  
Low birth weight (LBW)  
Gestational age (GA)  
Supplemental Therapeutic Oxygen for Prethreshold Retinopathy of Prematurity (STOP-ROP)  
High Oxygen Percentage in Retinopathy of Prematurity (HOPE-ROP)  
Surfactant, Positive Airway Pressure, Pulse Oximetry Randomized Trial (SUPPORT)

## Conflicts of Interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

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## Authors' contributions

PS updated the literature with the help of PubMed and wrote the manuscript with inputs from corresponding author (WA) all authors read and approved the final manuscript.

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