Scholars Journal of Applied Medical Sciences
Abbreviated Key Title: Sch J App Med Sci
ISSN 2347-954X (Print) | ISSN 2320-6691 (Online)
Journal homepage: https://saspublishers.com

OPEN ACCESS

PICU & Pediatrics

Effect of Nutritional Supplementation on Oxygen and Sepsis-Related Risk Factors for Retinopathy of Prematurity

Dr. Nasrin Akther[1*]

[1]Consultant, Department of PICU & Pediatrics, Ibn Sina Specialized Hospital, Dhaka, Bangladesh

DOI: https://doi.org/10.36347/sjams.2025.v13i07.019 | **Received:** 25.05.2025 | **Accepted:** 22.07.2025 | **Published:** 28.07.2025

***Corresponding author:** Dr. Nasrin Akther
Consultant, Department of PICU & Pediatrics, Ibn Sina Specialized Hospital, Dhaka, Bangladesh

Abstract | **Original Research Article**

Background: Retinopathy of prematurity (ROP) is a leading cause of childhood blindness, particularly in low- and middle-income countries. Oxygen therapy and septicemia are two of the most significant modifiable risk factors for ROP. Nutritional supplementation may reduce the incidence of these risk factors by supporting immune function and enhancing neonatal physiological stability. This study aimed to evaluate the effects of nutritional supplementation on oxygen and sepsis-related risk factors associated with ROP in preterm neonates. ***Methods:*** A randomized controlled trial was conducted from July 2018 to June 2020 at the Neonatology Department of Dhaka Shishu Hospital. A total of 150 preterm neonates (gestational age 32–34 completed weeks with peripheral avascular retinal zones on initial screening) were enrolled and randomized into two groups: supplementation (n=75) and control (n=75). Clinical parameters, including oxygen therapy, septicemia, respiratory distress, blood transfusion, and ROP status, were recorded. Data were analyzed using SPSS version 25.0, and a p-value ≤0.05 was considered statistically significant. ***Results:*** Oxygen therapy was required in 50.7% of the supplemented group compared to 76.0% in the control group (p=0.001). Septicemia occurred in 40.0% of supplemented neonates versus 58.7% of controls (p=0.022). ROP incidence was significantly lower in the supplemented group across subgroups with oxygen therapy, septicemia, and sex. ***Conclusion:*** Nutritional supplementation significantly reduces the need for oxygen therapy and the risk of developing septicemia in preterm neonates, thereby lowering the risk of ROP. Incorporating nutritional strategies into neonatal care protocols may be a valuable preventive approach.

Keywords: Retinopathy of prematurity, nutritional supplementation, oxygen therapy, sepsis, preterm neonates.

INTRODUCTION

Retinopathy of prematurity (ROP) is a Vaso proliferative condition of the retina, which has continued to be a major cause of childhood blindness in the world especially in preterm and LBW infants [1]. The occurrence of ROP can be prompted by the halting of normal retinal vascularization and subsequent pathological neovascularization owing to an array of perinatal risk factors, which comprise postnatal weight gains, oxygen therapy, sepsis and nutritional deficits [2,3].

The survival rate of preterm infants has been rising as a result of improvements in treating and caring about newborns, which have paradoxically increased the occurrence of ROP due to the lack of appropriate and comprehensive screening and follow-up interventions, especially in low- and middle-income countries [4]. ROP is a potentially emergent epidemic in such environments, worsened by uncontrolled oxygen treatments, sepsis and poor nutrition [5]. Bangladesh is a place where a large number of preterm infants develop ROP, and its development can be traced back to the system variables such as sepsis and oxygen therapy [6].

Nutritional status is one of the risk factors of ROP that can be modified. Normal retinal development is ensured by good postnatal nutrition that ameliorates the effects of oxidative stress and systemic inflammation, which are the most relevant in the pathogenesis of ROP [7]. An example that has protective properties against ROP is vitamin A because of its properties in maintaining epithelial integrity and regulation of vascularity [8]. A randomized trial carried out in Italy showed that the use of oral vitamin A supplementation decreased the incidence of ROP in very low birth weight babies [9]. Other nutrients are also needed in the prevention of oxidative harm and the enactment of immune competence such as protein, zinc, and antioxidants [10].

Sepsis, another critical risk factor, has been associated with an increased incidence and severity of ROP due to its pro-inflammatory state and vascular endothelial injury [11]. A systematic review by Wang et al. reported a significant association between neonatal sepsis and the development of ROP [12]. Similarly, oxygen therapy—though life-saving—can result in hyperoxia-induced retinal vessel damage, triggering abnormal neovascularization characteristic of advanced ROP stages [13].

Despite existing knowledge about these risk factors, studies evaluating the role of targeted nutritional interventions in reducing sepsis and oxygen dependence—and thereby indirectly mitigating ROP—remain limited in LMICs. Nutritional supplementation has the potential to improve neonatal immune responses and decrease the requirement for prolonged oxygen therapy, offering a low-cost strategy for ROP prevention.

This study aimed to evaluate the impact of nutritional supplementation on major risk factors for retinopathy of prematurity (ROP), focusing on the incidence of oxygen therapy and the incidence of septicemia in preterm neonates. By comparing the outcomes between the supplemented and non-supplemented groups, this study seeks to provide evidence for practical, low-cost interventions that can enhance neonatal care and reduce ROP risk in resource-limited settings.

METHODOLOGY & MATERIALS

This randomized controlled trial was conducted in the Neonatology Department of Dhaka Shishu Hospital over two years from July 2018 to June 2020. A total of 150 preterm neonates were enrolled and randomly assigned to either the supplemented group (n=75) or the control group (n=75). The study population included preterm neonates with gestational age between 32 and 34 completed weeks who presented with a peripheral avascular zone at their first ROP screening, regardless of gestational age.

Inclusion Criteria:

1. Preterm neonates with gestational age 32–34 completed weeks.
2. Presence of a peripheral avascular zone in the retina at first ROP screening.
3. Stable clinical condition allowing participation in nutritional supplementation protocol.

Exclusion Criteria:

1. Congenital ocular anomalies.
2. Major congenital malformations.
3. Neonates requiring prolonged invasive ventilation beyond 7 days.
4. Parental refusal to consent.

The study received approval from the Bangladesh Institute of Child Health. Informed written consent was obtained from all parents or legal guardians before enrollment. Data were prospectively collected using standardized forms and included demographic details, clinical findings, treatment modalities, and ROP status assessed via indirect ophthalmoscopy. Nutritional supplementation was administered according to protocol, and participants were monitored for oxygen therapy, septicemia, and other clinical outcomes. Data accuracy was ensured through double entry and regular verification. Statistical analysis was performed using SPSS version 25.0. Descriptive statistics summarized baseline characteristics, and inferential analyses, including chi-square and independent t-tests, assessed group differences. A p-value ≤0.05 was considered statistically significant. Participant confidentiality was strictly maintained throughout the study.

RESULTS

Table 1: Baseline Characteristics of Neonates in Supplemented and Control Groups (n=150)

Characteristic	Category	Supplemented (n=75)	Control (n=75)	p-value
Age (hours)	<24 hours	42 (56.0)	40 (53.3)	0.825
	24–48 hours	18 (24.0)	20 (26.7)	
	48–72 hours	15 (20.0)	15 (20.0)	
Mean ± SD		38.5 ± 19.2	39.7 ± 20.1	0.709
Sex	Male	39 (52.0)	42 (56.0)	0.612
	Female	36 (48.0)	33 (44.0)	
Birth Weight	1500–2000g	48 (64.0)	46 (61.3)	0.732
	1000–1499g	27 (36.0)	29 (38.7)	
Maternal HTN	Yes	23 (30.7)	21 (28.0)	0.717

Table 1 presents the demographic and clinical baseline characteristics of 150 preterm neonates in supplemented (n=75) and control (n=75) groups. The groups were matched for age at admission, sex distribution, birth weight, and maternal hypertension. The mean age (hours) was 38.5 ± 19.2 in the supplemented group and 39.7 ± 20.1 in the control group (p=0.709). Male neonates comprised 56% of the control group versus 52% of the supplemented group, though not statistically significant (p=0.612). Birth weights and maternal hypertension rates were comparable between groups (p=0.732 and p=0.717, respectively).

Table 2: Distribution of Clinical Risk Factors in Supplemented and Control Groups

Risk Factor	Supplemented (n=75)	Control (n=75)	p-value
Oxygen Therapy	38 (50.7)	57 (76.0)	0.001
Septicemia	30 (40.0)	44 (58.7)	0.022
Respiratory Distress	40 (53.3)	48 (64.0)	0.184
Blood Transfusion	20 (26.7)	31 (41.3)	0.06
Apgar Score <7 (1 min)	32 (42.7)	36 (48.0)	0.515

Table 2 shows key clinical risk factors for ROP in both groups. Oxygen therapy was given to 76.0% of control group neonates versus 50.7% in the supplemented group, a significant difference (p=0.001). Septicemia occurred in 58.7% of control neonates versus 40.0% of supplemented neonates (p=0.022). Respiratory distress and blood transfusion rates were lower in the supplemented group (53.3% and 26.7%) compared to controls (64.0% and 41.3%), though not statistically significant (p=0.184 and p=0.06). Apgar scores <7 at 1 minute were similar between groups (p=0.515).

Table 3: ROP Status by Risk Factor and Sex in Supplemented and Control Groups

Subgroup	ROP Status	Supplemented (n)	Control (n)
Oxygen Therapy	Present	19 (50.0)	45 (78.9)
	Absent	19 (50.0)	12 (21.1)
Septicemia	Present	19 (63.3)	37 (84.1)
	Absent	11 (36.7)	7 (15.9)
Male Neonates	Present	14 (35.9)	28 (66.7)
	Absent	25 (64.1)	14 (33.3)
Female Neonates	Present	10 (27.8)	22 (66.7)
	Absent	26 (72.2)	11 (33.3)

Table 3 describes ROP incidence by oxygen therapy, septicemia, and sex. Among neonates receiving oxygen therapy, 78.9% in the control group developed ROP, versus 50.0% in the supplemented group. For those with septicemia, 84.1% of control neonates developed ROP versus 63.3% in the supplemented group. Male neonates in the control group had higher ROP rates (66.7%) compared to the supplemented group (35.9%). Female neonates showed similar trends, with 66.7% in controls and 27.8% in the supplemented group developing ROP.

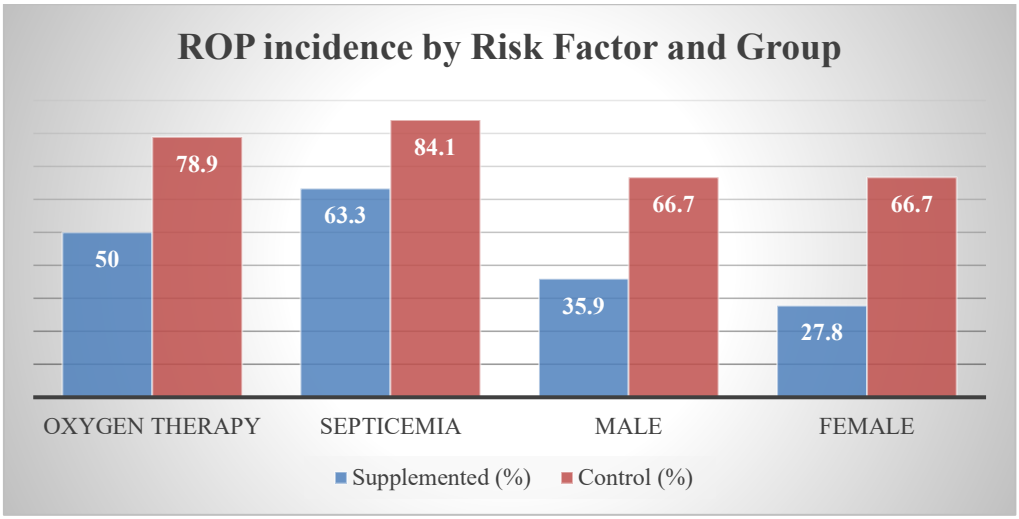

Figure 1: ROP Incidence by Risk Factor and Group

Figure 1 shows the incidence of ROP by risk factor—oxygen therapy, septicemia, and sex—in the supplemented and control groups. ROP rates were consistently lower in the supplemented group across all categories. The largest differences were observed among neonates with oxygen therapy and septicemia, where the control group had notably higher ROP incidence.

DISCUSSION

The present study shows a major correlation between nutritional supplementation to mitigate vital risk factors oxygen therapy and septicemia, which contributes to the development of retinopathy of prematurity (ROP) in premature babies. Particularly, the

supplemented group showed significantly reduced oxygen therapy (50.7% vs 76.0%) and septicemia (40.0% vs. 58.7%) compared to the control group. These results are consistent with the increasing body of evidence supporting the use of targeted nutritional interventions as a risk-reducing intervention against ROP since this has been shown to target underlying modifiable risk factors.

The influence of oxygen therapy in the pathogenesis of ROP has been well-documented. Hartnett and Lane pointed out that irregularities in oxygen exposure among premature children alter the normal processes of retinal vascularization, which causes pathologic neovascularization as a result of the downregulation of vascular endothelial growth factor (VEGF) to hyperoxia [13]. In the same regard, Estrada et al. found a dose-response effect between oxygen exposure and ROP incidence highlighting that careful use of oxygen is essential [3]. Our research supports these studies to argue a reduced presence of ROP among the neonates serviced with less oxygen treatment in the supplemented group. Nutritional support has the potential to increase respiratory efficiency and decrease the demand for supplemental oxygen and, subsequently, ROP risk.

Another significant cause of ROP is septicemia, which operates in an inflammatory mechanism and an oxidative mechanism. A meta-analysis by Wang et al. supported the strong correlation between neonatal sepsis and the development of the ROP, which is explained by the systemic inflammation and endothelial damage [12]. Dammann and Stansfield suggested that neovascularization of the retina supported sepsis since cytokines induced by sepsis may weaken the stability of the retinal vasculature [11]. The rates of septicemia were considerably lower and ROP correspondingly in the supplemented group indicating that nutritional support boosts immune defense and intestinal barrier functions and therefore limits the development of systemic infection.

Nutrient supplements are specifically applicable when there is poor postnatal growth in preterm infants, as well as in the immunological challenges of infants in LMICs. Hellstrm et al. insisted that early nutritional approaches could also play an important role in minimizing ROP through retinal growth and stability of the system [7]. Our results support this assertion in that supplemented neonates had a reduced risk of developing ROP, which is perhaps because of better weight gain, antioxidant defense, and immunity. Several micronutrients (vitamin A, zinc, essential fatty acids) have demonstrated potential in the regulation of ROP risk. Garofoli et al. showed that oral vitamin A decreased the incidence of ROP in very low birth weight infants [9]. Such low-risk and cost-effective interventions may be critical in Bangladesh, where ROP has become a threatening issue of public health.

Our research also found no gender disparities in the incidence of ROP, with male and female neonates of the supplemented group both having a lower prevalence of ROP than did their respective controls. Another study conducted by de las Rivas Ramirez et al. noted greater ROP risk in males, which could be attributed to sex distinctions in maturation of lung development; additionally, sex variations in VEGF expression [14]. These findings are consistent with our results and indicate that nutritional interventions may be beneficial in both genders, whereas the biological basis of this gender disparity should be investigated.

Furthermore, risk can be defined as the combination of multiple risk factors that compound ROP risk. Di Pietro et al. emphasized that respiratory distress and blood transfusion are comorbidities that predispose patients to ROP along with sepsis or oxygen treatment [15]. Although we did not find any significant effect on respiratory distress and transfusion rate, the decrease in primary risks (oxygen and sepsis) is probably the reason that contributed to a decrease in the risk of ROP in the supplemented group. That supports the multifactorial character of the ROP condition and the necessity of comprehensive preventative measures.

Importantly, our findings resonate with those of Fleck and McIntosh, who emphasized prevention over intervention for ROP in neonatal care, especially in resource-limited settings [16]. By addressing systemic factors such as nutrition and infection early, the burden of severe ROP requiring laser therapy or surgery can be substantially reduced.

However, this study has some limitations. The lack of long-term follow-up limits the conclusions on the progression or regression of ROP. Moreover, the study did not stratify supplementation components, making it difficult to determine the most effective nutrient(s) in the study. Future studies should investigate the specific contributions of micronutrients and their optimal doses.

Despite these limitations, this study presents strong evidence for the integration of nutritional strategies in neonatal care. Nutritional supplementation significantly reduces the need for oxygen therapy and the incidence of septicemia, which are two key risk factors for the development of ROP. These findings provide compelling evidence for incorporating nutritional interventions into standard neonatal care protocols, especially in LMICs, where resource constraints and high ROP burden coexist.

CONCLUSION

This study demonstrates that nutritional supplementation significantly reduces two major

modifiable risk factors for retinopathy of prematurity (ROP): oxygen therapy and sepsis. Preterm neonates receiving supplementation had lower incidences of both conditions, which translated into a lower overall risk of ROP development. These findings highlight the potential of targeted nutritional interventions as a cost-effective and scalable strategy for preventing ROP, particularly in resource-limited settings. This study emphasizes the need to integrate nutritional protocols into neonatal care pathways to improve clinical outcomes and reduce the burden of ROP-related visual impairment in preterm infants.

Conflicts of interest

There are no conflicts of interest.

Ethical approval

The study was approved by the Institutional Ethics Committee.

REFERENCES

1. Gilbert C. Retinopathy of prematurity: a global perspective of the epidemics, population of babies at risk and implications for control. Early human development. 2008 Feb 1;84(2):77-82.
2. Cavallaro G, Filippi L, Bagnoli P, La Marca G, Cristofori G, Raffaeli G, Padrini L, Araimo G, Fumagalli M, Groppo M, Dal Monte M. The pathophysiology of retinopathy of prematurity: an update of previous and recent knowledge. Acta ophthalmologica. 2014 Feb;92(1):2-0.
3. Estrada MM, Tomlinson LA, Yu Y, Ying GS, Binenbaum G. Daily oxygen supplementation and risk of retinopathy of Prematurity. Ophthalmic Epidemiology. 2023 May 4;30(3):317-25.
4. Ahmed AN, Muslima H, Anwar KS, Khan NZ, Chowdhury MA, Saha SK, Darmstadt GL. Retinopathy of prematurity in Bangladeshi neonates. Journal of tropical pediatrics. 2008 Oct 1;54(5):333-9.
5. Mannan MA. Frequency and risk factors of retinopathy of prematurity among preterm neonates in a tertiary care hospital of Bangladesh. Journal of Clinical Pediatrics and Neonatology. 2023 Nov 29;3(1):11-7.
6. Liton CS, Mahbubul H, Dipak KN, Azad CM. Screening for retinopathy of prematurity in neonatal Unit-An experience of a tertiary care hospital in Bangladesh. Acad J Ped Neonatol. 2017;3(3):555612.
7. Hellström A, Kermorvant-Duchemin E, Johnson M, Sáenz de Pipaón M, Smith LE, Hård AL, ESPR Nutrition council members Fusch Christoph 7 8 Iacobelli Silvia 9 Johnson Mark J. 4 10 Lapillonne Alexandre 11 12 Moltu Sissel J. 13 Sáenz de Pipaón Miguel 14 Zachariassen Gitte 15 16. Nutritional interventions to prevent retinopathy of prematurity. Pediatric Research. 2024 Sep;96(4):905-11.
8. Mactier H, McCulloch DL, Hamilton R, Galloway P, Bradnam MS, Young D, Lavy T, Farrell L, Weaver LT. Vitamin A supplementation improves retinal function in infants at risk of retinopathy of prematurity. The Journal of pediatrics. 2012 Jun 1;160(6):954-9.
9. Garofoli F, Barillà D, Angelini M, Mazzucchelli I, De Silvestri A, Guagliano R, Decembrino L, Tzialla C. Oral vitamin A supplementation for ROP prevention in VLBW preterm infants. Italian Journal of Pediatrics. 2020 Dec; 46:1-4.
10. Uberos J, Miras-Baldo M, Jerez-Calero A, Narbona-López E. Effectiveness of vitamin A in the prevention of complications of prematurity. Pediatrics & Neonatology. 2014 Oct 1;55(5):358-62.
11. Dammann O, Stansfield BK. Neonatal sepsis as a cause of retinopathy of prematurity: an etiological explanation. Progress in retinal and eye research. 2024 Jan 1; 98:101230.
12. Wang X, Tang K, Chen L, Cheng S, Xu H. Association between sepsis and retinopathy of prematurity: a systematic review and meta-analysis. BMJ open. 2019 May 1;9(5):e025440.
13. Hartnett ME, Lane RH. Effects of oxygen on the development and severity of retinopathy of prematurity. Journal of American Association for Pediatric Ophthalmology and Strabismus. 2013 Jun 1;17(3):229-34.
14. de las Rivas Ramírez N, Luque Aranda G, Rius Díaz F, Pérez Frías FJ, Sánchez Tamayo T. Risk factors associated with retinopathy of prematurity development and progression. Scientific Reports. 2022 Dec 20;12(1):21977.
15. Di Pietro M, Decembrino N, Afflitto MG, Malerba E, Avitabile T, Franco LM, Longo A, Betta P. Risk factors in the development of retinopathy of prematurity: A 10-year retrospective study. Early Human Development. 2023 Oct 1; 185:105844.
16. Fleck BW, McIntosh N. Pathogenesis of retinopathy of prematurity and possible preventive strategies. Early human development. 2008 Feb 1;84(2):83-8.