Clinical and Risk Factor Profile of Infants Treated with Bevacizumab or Nd: YAG Laser for Retinopathy of Prematurity

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**Abstract**

**Background:** Retinopathy of prematurity is a major cause of avoidable childhood blindness, particularly in premature infants with low birth weight and early gestational age. Both intravitreal Bevacizumab and Nd: YAG laser are established treatments for type 1 and aggressive posterior retinopathy of prematurity, but limited data exist comparing the clinical characteristics of infants receiving these therapies. This study aimed to compare the clinical and risk factor profiles of infants treated with intravitreal Bevacizumab versus Nd: YAG laser for retinopathy of prematurity.

**Methods:** This prospective observational study was conducted over one year at two tertiary care hospitals in Dhaka, Bangladesh. A total of 61 infants (122 eyes) diagnosed with type 1 ROP or AP-ROP were enrolled. Patients were assigned to receive either intravitreal bevacizumab or Nd: YAG laser therapy. Baseline characteristics, delivery history, and perinatal risk factors such as apnea, sepsis, RDS, jaundice, and blood transfusions were recorded. Data were analyzed using SPSS v20 with chi-squared testing for categorical variables and significance set at p < 0.05.

**Results:** The mean gestational age and birth weight were slightly lower in the intravitreal bevacizumab group than in the laser group, though not statistically significant. Sex distribution, delivery method, and presence of neonatal risk factors were comparable across both groups. No significant differences were found in any risk parameter.

**Conclusion:** Infants treated with intravitreal bevacizumab and laser for retinopathy of prematurity showed similar clinical and risk profiles. Treatment decisions appear more influenced by procedural and institutional factors than by patient-specific characteristics.

**Keywords:** Retinopathy of prematurity, Bevacizumab, Nd: YAG laser, gestational age

**Introduction**

Retinopathy of prematurity (ROP) is a pathological proliferation process of the vasculature in a developing retina in a preterm infant and is still one of the most serious sources of treatable blindness in children globally. It is mainly associated with low-weight neonates by the fetus of premature gestational age [1,2]. The prevalence of ROP has declined in high-income countries with the improvements in neonatal care, but in low- and middle-income countries, the prevalence is on the rise because the number of preterm babies surviving has increased, but the patient outcome has not improved due to a lack of neonatal care and screening strategies [1,3].

The main characteristics of ROP pathogenesis are disorganized retinal vascular growth. A sudden shift in changes when premature infants exist intrauterinely and extrauterinely causes a maladjustment of oxygen responses and overexpression of vascular endothelial growth factor, also known as VEGF, which contributes to the development of pathological neovascularization [4]. The identified risk factors of ROP are low birth weight, low gestational age, oxygen therapy, respiratory distress syndrome (RDS), sepsis, apnea and repeated blood transfusions [5,6].

Such interventions as cryotherapy and panretinal photocoagulation (PRP) with diodes or Nd: YAG lasers are historically considered standard interventions used to treat ROP [7]. Although laser treatment works well to destroy the peripheral retina that is avascular and decrease the level of VEGF production, laser treatment destroys healthy retinal tissue and causes peripheral visual field loss as well as high refractive error in the advanced years [8].

During the last years, the use of intravitreal anti-VEGF agents, including bevacizumab appeared to become a promising alternative treatment of type 1 and aggressive posterior ROP (AP-ROP). The BEAT-ROP trial was crucial in confirming the high strength of efficacy of intravitreal bevacizumab (IVB) as compared to traditional laser therapy, especially in zone I disease [9]. Anti-VEGF treatment can prevent peripheral retinal degeneration and is correlated with reduced myopia, but it is still suspected that there will be untoward effects with systemic VEGF repression and the neurodevelopmental consequences [10,11].

Although multiple studies have compared the efficacy and outcomes of laser and IVB treatments, limited data exist on the underlying clinical and risk factor profiles of infants receiving these therapies, especially in resource-constrained settings. Understanding the demographic and clinical characteristics of infants treated with IVB or laser is essential for optimizing treatment protocols and identifying infants at higher risk for severe ROP.

This study was conducted at tertiary neonatal care centers in Bangladesh, where both IVB and Nd: YAG lasers are routinely used for ROP management. The aim was to evaluate and compare the clinical characteristics and perinatal risk factors among infants treated with either IVB or Nd: YAG laser. By examining parameters such as gestational age, birth weight, sex, mode of delivery, and systemic conditions like sepsis and RDS, this study contributes to a more nuanced understanding of treatment allocation and patient risk stratification in real-world clinical practice.

**Methodology & Materials**

This prospective observational study was conducted from January 2018 to December 2018 at the Department of Vitreo-Retina and Pediatric Ophthalmology, National Institute of Ophthalmology and Hospital, as well as in the Special Care Baby Unit (SCABU) and ICU at Dhaka Shishu Hospital, Bangladesh. A total of 61 infants (122 eyes) diagnosed with type 1 or aggressive posterior retinopathy of prematurity (ROP) were included.

**Sample Selection**

**Inclusion Criteria:**

* Infants diagnosed with Type 1 ROP
* Infants diagnosed with Aggressive Posterior ROP (AP-ROP)

**Exclusion Criteria:**

* Neonates clinically unfit for procedures (e.g., failure to thrive)
* Infants with Stage 5 ROP
* Infants with congenital heart disease

**Data collection and study procedure:**

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For IVB, the injection was administered 1 to 1.5 mm posterior to the limbus using a 30-gauge needle under sterile conditions. Nd: YAG laser (1064 nm wavelength) photocoagulation was performed with indirect ophthalmoscopy after adequate pupillary dilation and local anesthesia. Clinical data, including gestational age, birth weight, sex, laterality of eye involvement, birth history, and perinatal risk factors, were documented. Confidentiality and voluntary participation were ensured, and participants could withdraw from the study at any time without affecting their standard care. Statistical analysis was performed using SPSS version 20. Categorical variables were compared using the chi-squared test, and continuous variables using mean ± standard deviation. A p-value < 0.05 was considered statistically significant.

**Results**

A total of 122 eyes from 61 infants diagnosed with retinopathy of prematurity (ROP) were evaluated for clinical and risk factor profiles between two treatment groups: intravitreal Bevacizumab (IVB) and Nd: YAG laser. Key demographic, perinatal, and clinical characteristics are summarized below.

**Figure 1: Distribution of children of ROP between two treatment group (IVB treated group and laser treated group)**

Among 122 eyes of 61 infants of ROP, 60 eyes of 30 infants treated with intravitreal Bevacizumab (IVB) and 62 eyes of 31 infants treated with Nd: YAG laser (Fig-1).

**Figure 2: Sex distribution of children of ROP between two treatment group (IVB treated group and laser treated group)**

Sex distribution of the study subjects shows that in IVB group out of 30 infants 15 were male and 15 were female, laser group out of 31 infants 15 were male and 16 were female (Fig. 2).

**Table 1: Baseline characteristics of infants treated with intravitreal Bevacizumab and Nd: YAG laser**

|  |  |  |  |
| --- | --- | --- | --- |
| **Characteristics** | **Bevacizumab Group** | **Laser Group** | **P value** |
| **Gestational age in weeks** | **<28** | 3 (10.0%) | 7 (22.6%) |  |
| **28- 32** | 23 (76.7%) | 21 (67.7%) |
| **>32** | 4 (13.3%) | 3 (9.7%) |
| **Mean±SD** | 29.12±2.04 | 30.55±2.4 | 0.285 |
| **Birth weight in grams** | **Mean±SD** | 1332±214.45 | 1394±322.19 | 0.317 |
| **Sex distribution** | **Male** | 15(50%) | 10(32.3%) | 0.675 |
| **Female** | 15(50%) | 21(67.7%) | 0.782 |
| **Laterality of involvement (Both eyes)** | 30(100%) | 31(100%) | 0.762 |
| **Birth history** | **Normal vaginal delivery** | 20(66.7%) | 25(80.6%) | 0.451 |
| **Ceaserian section** | 10(33.3%) | 06(19.4%) | 0.633 |

Table 1 presents the baseline characteristics of infants treated with IVB and Nd: YAG laser. The mean gestational age was 29.12 ± 2.04 weeks in the IVB group and 30.55 ± 2.4 weeks in the laser group (p = 0.285). The mean birth weight was 1332 ± 214.45 g in the IVB group and 1394 ± 322.19 g in the laser group (p = 0.317). Both groups had nearly equal sex distribution and bilateral eye involvement. Birth history showed a similar number of infants born via normal vaginal delivery (NVD) and cesarean section (CS) across groups.

**Table 2: Presence of following risk factors in infants treated with intravitreal Bevacizumab and Nd: YAG laser**

|  |  |  |  |
| --- | --- | --- | --- |
| **Risk factors** | **Bevacizumab Group** | **Laser Group** | **P value** |
| Oxygen inhalation | 30 | 31 | 0.235 |
| Septicemia | 3 | 2 | 0.417 |
| Apnea | 7 | 8 | 0.324 |
| RDS | 7 | 7 | 0.412 |
| Neonatal jaundice | 10 | 11 | 0.513 |
| Blood transfusion | 2 | 3 | 0.298 |

Table 2 describes the presence of perinatal risk factors in both groups. Oxygen inhalation was documented in all infants (100%) in both groups. Other conditions included septicemia (3 IVB vs 2 laser), apnea (7 IVB vs 8 laser), respiratory distress syndrome (RDS) in 7 infants from each group, neonatal jaundice (10 IVB vs 11 laser), and need for blood transfusion (2 IVB vs 3 laser). None of the differences between groups were statistically significant.

**Discussion**

This study compared the clinical and perinatal risk factor profiles of infants with retinopathy of prematurity (ROP) treated with either intravitreal Bevacizumab (IVB) or Nd: YAG laser photocoagulation. The findings indicate no significant differences between the two treatment groups in terms of gestational age, birth weight, sex distribution, delivery method, or comorbid neonatal conditions. These results support the growing consensus that the choice of treatment is often dictated by institutional protocols and physician discretion rather than patient-specific risk factor profiles.

The two most established risk factors in the development and severity of ROP include gestational age and birth weight. In our study, the average gestation and birth weight of the IVB group was slightly lower than the laser group, but the difference was not found to be significant. This is consistent with results proved by Mintz-Hittner et al., who showed that in more immature infants or those with aggressive posterior ROP (AP-ROP), an IVB was frequently selected because of a less intrusive procedure with a fast reaction [9].

The distribution of sex in both groups was almost equal, and this is in line with the results of Castellanos et al. and Hwang et al., who were unable to identify the effect of sex on the development and treatment of ROP [6,12]. All the babies had bilateral involvement of ROP, typical of the severe disease or requirement of treatment [3].

In terms of delivery means, the number of infants who were born through a normal vaginal delivery (NVD) and a cesarean section (CS) was rather similar in both groups. Although there is some literature that indicates that CS may hold the risk of ROP at bay because it results in reduced birth trauma and more efficient oxygen control at birth [13], it turns out that the mode of delivery is not a significant factor in terms of allocation of treatment.

Both groups had similar frequencies with neonatal complications of oxygen therapy, apnea, respiratory distress syndrome (RDS), neonatal jaundice, sepsis and the presence of blood transfusions. Oxygen treatment was demanded, without exception, thus pointing to the fact that it is not only a life-saving measure and an important risk factor of ROP. The connection between long-term oxygen exposure and retinal neovascularization has been previously highlighted in other studies [5].

The proportion of apnea and RDS were almost equal in the two groups, and this fact showed that the respiratory morbidity was a common background reason regardless of the type of treatment. The current results conform to the results recorded by Ahmed et al., who highlighted the inability of systemic neonatal conditions to dictate the type of treatment, though it may affect prognosis [14].

The implication of sepsis and neonatal jaundice as additive risk factors in the development of ROP has been documented well. They are supported by our findings and lack meaningful group differences, in line with the results of Yoon et al. [15]. Less frequent but a little more prevalent in the laser group were blood transfusions. It has been indicated that transfusion might elevate the severity of ROP, possibly due to the changing oxygen saturation rates and iron overload [2].

In spite of the matching characteristics and risk profile, the treatment strategy is still inconsistent across the centers and often correlated with local experience, availability of equipment, and preference of physicians. Over the last few years, IVB has become a popular method because of its apparent ease of administration, less procedural time and minimal anesthetic needs; thus, it is used particularly to perform on fragile neonates [16.17]. There are still some questions concerning systematic VEGF inhibition and prolonged neurodevelopmental effects, particularly with intermittent dosing [11,18].

On the other hand, laser photocoagulation is the long-term standard and has decades-long follow-up data on visual and refractive outcomes [19]. Despite being more invasive, it is a stable method, especially when the follow-up could not be checked very well; the risk of late recurrence with it is lower than with IVB [20].

The work confirms once more that not only in IVB but also in laser-treated infants, the clinical and risk profiles of patients are similar enough, and thus the treatment process is unlikely to depend on demographics and comorbidities. Instead, the choice is shaped more by logistical and procedural factors, and increasingly by considerations around long-term systemic safety and parental preference.

Understanding the risk factor profiles of infants receiving either treatment provides valuable insight into how clinical decisions are made in practice and ensures that infants with similar baseline characteristics receive consistent standards of care.

**Conclusion**

This study found no significant differences in clinical and perinatal risk factor profiles between infants treated with intravitreal Bevacizumab and those treated with Nd: YAG laser for retinopathy of prematurity. Gestational age, birth weight, sex, delivery method, and systemic neonatal conditions were comparably distributed across both groups. These findings suggest that treatment modality is influenced more by physician discretion and institutional logistics than by specific patient characteristics. A standardized assessment of clinical profiles can support consistent treatment decisions and inform future strategies for early risk-based interventions in ROP care, especially in low-resource settings.

Consent:

Written informed consent was obtained from the parents or legal guardians of all infants. Eligible infants received either intravitreal Bevacizumab (0.625 mg/0.025 mL) or Nd: YAG laser photocoagulation based on the clinical scenario and the physician’s discretion.

Disclaimer (Artificial intelligence)

Option 1:

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

**References**

1. Gilbert C. Retinopathy of prematurity: a global perspective of the epidemics, population of babies at risk and implications for control. Early Hum Dev. 2008;84(2):77–82.
2. Hartnett ME, Penn JS. Mechanisms and management of retinopathy of prematurity. N Engl J Med. 2012;367(26):2515–26.
3. Quinn GE, et al. Visual acuity of eyes after vitrectomy for retinopathy of prematurity: follow-up at 5 1/2 years. Ophthalmology. 1996;103(4):595–600.
4. Alon T, et al. Vascular endothelial growth factor acts as a survival factor for newly formed retinal vessels and has implications for retinopathy of prematurity. Nat Med. 1995;1(10):1024.
5. Smith LE. Through the eyes of a child: understanding retinopathy through ROP, the Friedenwald lecture. Invest Ophthalmol Vis Sci. 2008;49(12):5177–82.
6. Castellanos MAM, et al. Short-term outcome after intravitreal ranibizumab injections for the treatment of retinopathy of prematurity. Br J Ophthalmol. 2013;97(7):816–9.
7. Capone Jr A, et al. Diode-laser photocoagulation for zone 1 threshold ROP. Am J Ophthalmol. 1993;116(4):444–50.
8. Harder BC, et al. Intravitreal bevacizumab for ROP: refractive error results. Am J Ophthalmol. 2013;155(6):1119–24. e1.
9. Mintz-Hittner HA, Kennedy KA, Chuang AZ. Efficacy of intravitreal bevacizumab for stage 3+ ROP. N Engl J Med. 2011;364(7):603–15.
10. Mireskandari K, Adams GG, Tehrani NN. Recurrence of ROP following bevacizumab monotherapy. JAMA Ophthalmol. 2013;131(4):544–5.
11. Zayek M, et al. Bevacizumab for ROP: 2-year neurodevelopmental follow-up. Am J Perinatol. 2020; 38:1158 66.
12. Hwang, C.K., et al., Outcomes after intravitreal bevacizumab versus laser photocoagulation for retinopathy of prematurity: a 5-year retrospective analysis. Ophthalmology, 2015. 122(5): p. 1008-1015.
13. Martínez-Castellanos, M.A., et al., Long-term effect of antiangiogenic therapy for retinopathy of prematurity up to 5 years of follow-up. Retina, 2013. 33(2): p. 329-338.
14. Ahmed K, Ali AS, Delwadia N, Greven MA. Neurodevelopmental outcomes following intravitreal bevacizumab with laser versus laser photocoagulation alone for retinopathy of prematurity. Ophthalmic Surgery, Lasers and Imaging Retina. 2020 Apr 1;51(4):220-4.
15. Yoon JM, Shin DH, Kim SJ, Ham DI, Kang SW, Chang YS, Park WS. Outcomes after laser versus combined laser and bevacizumab treatment for type 1 retinopathy of prematurity in zone I. Retina. 2017 Jan 1;37(1):88-96.
16. Chung, E.J., et al., Combination of laser photocoagulation and intravitreal bevacizumab (Avastin®) for aggressive zone I retinopathy of prematurity. Graefe's Archive for Clinical and Experimental Ophthalmology, 2007. 245(11): p. 1727.
17. Nazari, H., et al., Intravitreal bevacizumab in combination with laser therapy for the treatment of severe retinopathy of prematurity (ROP) associated with vitreous or retinal hemorrhage. Graefe's Archive for Clinical and Experimental Ophthalmology, 2010. 248(12): p. 1713-1718.
18. Rodriguez SH, Blair MP, Shapiro MJ, Berrocal AM, Murray TG, Martinez-Castellanos MA, Hubbard III GB. Neurodevelopmental outcomes of preterm infants with retinopathy of prematurity by treatment. Pediatrics. 2020 Apr 1;145(4):e20200056A.
19. Yang, C., et al., Long-term visual outcomes of laser-treated threshold retinopathy of prematurity: a study of refractive status at 7 years. Eye, 2010. 24(1): p. 14.
20. Hu, J., et al., Reactivation of retinopathy of prematurity after bevacizumab injection. Archives of ophthalmology, 2012. 130(8): p. 1000-1006.