
*Original Article*LASER PHOTOCOAGULATION VERSUS INTRAVITREAL ANTI VEGF AGENTS
FOR TREATMENT OF RETINOPATHY OF PREMATURITY

Aldghaimy, A.

Ophthalmology dept., Faculty of Medicine, South Valley, Univ., Egypt,

E-mail: adghaimy@yahoo.com

Received: 29/1/2024

Accepted: 19/4/2024

Doi: 10.21608/ejco.2024.361193

Abstract

Background: Early birth and various oxygen techniques can cause retinopathy of prematurity (ROP), a widespread childhood visual problem. An aggressive ROP (A-ROP) differs from normal progression. Diode laser replaced cryotherapy. Laser treatment is customary but limited, prompting anti-VEGF research. BEAT-ROP aids anti-VEGF. **Aim:** Compare efficacy and safety of laser photocoagulation with intravitreal anti-VEGF agents for ROP. **Methods:** Retrospective study at Qena university hospital, adhering to Helsinki Declaration. Participants had ROP type 1 or A-ROP, treated with anti-VEGF or laser within 72 hours (or 24 hours for A-ROP) between 2021 and 2024 at Qena University, followed for ≥ 6 months. ICROP criteria guided diagnosis and classification. Treatment decision involved parental consultation; unfit patients for general anesthesia received anti-VEGF. Patients anticipated to have poor adherence to follow up received anti-VEGF. Post-treatment follow-ups evaluated efficacy, with cycloplegic refraction at 6 months. Outcome measures included regression, reactivation, and retinal detachment. **Results:** Significant differences observed between Anti-VEGF and Laser groups in Zone-I ROP and APROP parameters. No significant variation in sex distribution, gestational age (GA), birth weight, or follow-up duration in Zone-I. In Zone-II, significant differences in GA, birth weight, and follow-up duration. Anti-VEGF demonstrated superior outcomes in initial regression, reactivation, and retinal detachment. **Conclusion:** Anti-VEGF therapy, notably Ranibizumab, outperforms laser photocoagulation for ROP treatment in aggressive forms in Zone I. This appears to show better initial regression, lesser reactivation, and lower retinal detachment. Anti-VEGF therapy, and laser photocoagulation for ROP treatment in Zone II appears to show comparable initial regression and retinal detachment but laser show lesser reactivation than Anti-VEGF therapy. Research in clinical practice is needed.

Keywords: Laser photocoagulation, Intravitreal anti-VEGF agents, Retinopathy of prematurity, Ocular therapy.

1. Introduction

Retinopathy of prematurity (ROP) is a major cause of visual impairment in children globally, regardless of their developmental level. This syndrome is highly correlated

with premature delivery and changes in procedures for administering oxygen. Aggressive retinopathy of prematurity (A-ROP) is a specific subtype of ROP that

is mainly seen in premature newborns. It is defined by a fast advancement of the illness, which is different from the usual stages of ROP [1]. In the last thirty years, there have been significant advancements in the treatment approaches for ROP. The CRYO-ROP study initially established the efficacy of cryotherapy, establishing a significant standard [2]. The Early Treatment for Retinopathy of Prematurity (ETROP) randomized study demonstrated the advantages of diode laser therapy for retinal disorders. At present, laser therapy is widely used as a standard approach to control ROP [3]. Nevertheless, progress in comprehending the causes of ROP and acknowledging the constraints of laser therapy have prompted the investigation of alternate therapies. Anti-vascular endothelial growth factor (anti-VEGF) therapy has recently gained attention as a potentially effective additional treatment method [4]. Bevacizumab (IVB), ranibizumab (IVR), and conbercept (IVC) are anti-VEGF medications that have been shown to effectively inhibit the progression of retinopathy of prematurity (ROP). This was established in the Bevacizumab Eliminates the Angioge-

2. Methods

An investigation into the past was carried out at Qena University Hospital after receiving approval from the Clinic Institutional Review Board. The principles that are established in the Declaration of Helsinki were adhered to throughout the course of this research project. Patients were considered for participation in the study if they had been diagnosed with either type 1 retinopathy of prematurity (ROP) or aggressive retinopathy of prematurity (A-ROP) and had received treatment with anti-vascular endothelial growth factor (anti-VEGF) agents, specifically ranibizumab, or laser photocoagulation within the first 72 hours after receiving their diagnosis (24 hours for A-ROP). The research in issue was conducted at Qena University between the years 2021 and 2024 acco-

rding to the relevant research. Their care and supervision of the patients lasted for a minimum of six months over the course of their treatment. The diagnosis of ROP as well as the classification of ROP were both performed by the application of the international categorization of ROP (ICROP, 2005). There were certain criteria that were utilized in the Early Treatment Retinopathy of Prematurity Study (ETROP, 2003) in order to arrive at a diagnosis of type 1 ROP. All of the requirements that are included in this group are as follows: Zone I with any stage of ROP accompanied by plus disease, Zone I stage 3 without plus disease, or Zone II stage 2 or stage 3 with plus disease. A-ROP was characterized by the enlargement and twisting of arteries in the back part of the

eye in all four areas, as well as the development of a novel network of blood vessels between areas of the retina that have blood vessels and areas that do not have blood vessels in Zone I and the back part of Zone II (ETROP, 2003). This was the case in all four areas of the eye. The situation was the same in each of the four regions of the eye. As a result of the meetings that were held with the parents or guardians of infants who were diagnosed with ROP, treatment regimens were devised. Anti-VEGF injections were the most popular method of treatment for patients who were not candidates for general anesthesia. This was because these injections were administered to patients. Both topical and inhalation anesthetics were applied in order to facilitate the administration of the injections in a more straightforward manner. After the administration of a solution that included 10% povidone-iodine, an eyelid speculum was utilized in order to separate the eyelid and maintain its open position. After this, the eyelid was treated with the solution before the procedure was completed. There was a dosage of 0.25 mg/0.025 ml of the pharmaceutical Ranibizumab (IVR) that was administered using a sterile needle with a diameter of 30 gauge. This was done in order to ensure that the medication was administered correctly. In order to enter the needle, it was brought to within one millimeter of the limbus. During the laser photocoagulation treatments that were carried out, either inhalation or intubation anesthesia was applied as a method of medical administration. It was necessary to employ a device known as an eyelid speculum in order to keep the eyelids open. Additionally, a specialized laser known as an indirect laser (IRIDEX LIO Plus 810 nm - Large Spot) was applied in order to apply controlled heat to the avascular retina in order to treat the disease. A follow-up examination was performed on the patients the following day, following the administration of either an anti-VEGF injection

or laser photocoagulation. The purpose of this examination was to detect whether or not the patients displayed any signs of infection. It was decided that further appointments would be arranged either one week after the treatment or two weeks after the laser therapy. These visits would take place after the injection. The success of the treatment was going to be evaluated at these appointments, which were scheduled. The patient was scheduled to attend further sessions in the future, their schedule being determined by the stage of pregnancy they were now in as well as the state of their eyes. There were three further operations that were carried out during the follow-up period. These procedures included reinjection, supplemental laser therapy, external compression, and vitrectomy with or without lensectomy. Initial regression, reactivation that necessitated retreatment, and retinal detachment were the key criteria that were utilized for the purpose of assessment. The phrase "initial regression" is used to describe the partial or whole regression of an illness or condition that happened after the initial medicine was delivered. This can be a beneficial or detrimental effect. The appearance of retinal detachment is an indicator that the patient has proceeded to stage 4a or 4b ROP or stage 5 ROP, which necessitates vitrectomy with or without lensectomy. This is the case when the patient has reached this level. The term "reactivation" refers to the reappearance of plus illness or ridge, and it is described as the process that necessitates retreatment. In order to complete the process of reactivation, retreatment is required. The patient characteristics that were included in the data that was collected for the study were as follows: gender, gestational age at birth, birth weight, ROP zone and stage, presence of plus disease or A-ROP, age at initial therapy, duration of follow-up, presence of reactivation, and receipt of subsequent therapies. The data was collected for the purpose of the study.

2.1. Patient classification

The eyes were divided into two major groups according to the exact kind and subtype of retinopathy of prematurity (ROP), which was the condition that was diagnosed. The first group consisted of 110 eyes that had been diagnosed with aggressive retinopathy of prematurity (A-ROP) and Zone I ROP, both of which did not match the diagnostic criteria for type 1. The second group consisted of 160 eyes that had retinopathy of prematurity (ROP) with plus disease and were classified as Zone II stage 2 or stage 3.

2.2. Statistical analysis

The dataset was subjected to statistical analysis using SPSS software (version 22; SPSS Science, Chicago, IL). Numerical data were compared using the Mann-Whitney U-test and Student's t-test, while categorical data were assessed using the Chi-square test. For evaluating binary treatment outcomes for zone II type retino-

One of these groups was treated with anti-vascular endothelial growth factor (anti-VEGF) drugs, while the other group was subjected to laser photocoagulation. These groups were then subdivided into two subgroups. Comparative studies were carried out in order to evaluate the rates of initial regression, reactivation that required retreatment, and the incidence of retinal detachment that required surgical intervention among the subgroups that were contained within each major group.

pathy of prematurity (ROP) and considering the correlation between eyes, a generalized estimating equation (GEE) technique was employed. The GENMOD function from SAS version 9.4, developed by SAS Institute in Cary, NC, was utilized for this purpose. A p-value of less than 0.05 was considered statistically significant.

3. Results

Notable differences in the distribution of sexes were seen in the study that compared the groups that received Anti-VEGF and Laser therapies for the treatment of Zone I retinopathy of prematurity (ROP) and aggressive ROP (APROP). The statistical significance of these differences was determined to be 0.37. While the percentage of males in the Laser group was 43.75 percent, the percentage of males in the Anti-VEGF group was 53.85 percent. On the other hand, the percentage of females in the Anti-VEGF group was 46.15 percent, whereas the percentage of females in the Laser group was 56.25 percent, representing a p-value of 0.33. The average values of the gestational age (GA) were 29.55 ± 1.71 weeks in the Anti-VEGF group and 29.59 ± 1.69 weeks in the Laser group. This indicates that there was no significant difference between the groups in terms of GA ($p= 0.9$). While the Anti-VEGF group had a mean birth weight of

1344.08 ± 194.44 grams, the Laser group had a mean birth weight of 1372.75 ± 204.17 grams. This indicates that there was no significant difference in birth weight between the two groups ($p= 0.5$). A statistical analysis revealed that there was no significant difference in the duration of follow-up between the two groups ($p= 0.87$). The Anti-VEGF group had mean durations of 17.27 ± 3.83 months, whereas the Laser group had mean durations of 17.14 ± 3.23 months. The distribution of sexes in the groups that received Anti-VEGF and Laser treatments did not differ significantly from one another when the Rate of Progression (ROP) in Zone II was analyzed ($p= 0.987$). All of the groups received the same amount of therapy. In the group that was given anti-VEGF medication, there were 51.92% male participants and 48.08% female individuals. In comparison, the Laser group consisted of 48.21% females and 51.79% males

throughout its membership. The group that received Anti-VEGF had an average gestational age of 28.86 ± 1.47 weeks, whereas the group that received Laser had an average of 30.45 ± 1.69 weeks. Important differences were seen in the gestational age, with a p-value of less than 0.0001. In comparison to the Laser group, which had a birth weight of 1453.2 ± 279.04 grams, the Anti-VEGF group had a significantly lower birth weight ($p < 0.0001$), with an average of 1290.44 ± 269.83 grams born to that group. Furthermore, it is worth noting that the duration of follow-up was significantly shorter in the Anti-VEGF group ($p < 0.0001$), with an average number of 18.79 ± 8.22 months, in contrast to the Laser group, which had a duration of 24.89 ± 13.18 months, tab. (1). When the treatment results for Zone I ROP and APROP were compared between Anti-VEGF and Laser therapy, it was found that there were significant differences identified in a number of metrics. Surprisingly, a much higher percentage of patients in the Anti-VEGF group showed signs of improvement in compared to those in the Laser group ($p = 0.0179$). To be more specific, 83.33 percent of patients in the Anti-VEGF group saw early regression, but only 62.45 percent of patients in the Laser group showed similar regression. In addition, the frequency of condition reactivation was less common

in the Anti-VEGF group compared to the Laser group, although this difference did not achieve statistical significance ($p = 0.1145$), with reactivation rates of 28.2% and 43.75%, respectively. As an additional point of interest, the Anti-VEGF group saw a lower incidence of retinal detachment in comparison to the Laser group. Nevertheless, this disparity did not approach the level of statistical significance ($p = 0.0681$), with rates of 5.13% and 15.63% representing the corresponding groups. During the process of evaluating the efficacy of Anti-VEGF and Laser therapy in Zone II ROP, it was observed that there was no significant difference in the first regression rates between the Anti-VEGF and Laser groups ($p = 0.6711$). The respective rates were 97.13% and 98.21% and were not significantly different from one another. However, it is worth noting that the reactivation rate in the Anti-VEGF group was significantly lower compared to the Laser group ($p < 0.017$). The rates of 5.36% and 19.23%, respectively, were seen in the both groups. However, there was no significant difference in the incidence of retinal detachment between the two groups ($p = 0.6545$), with rates of 0.96% for the Anti-VEGF group and 1.79% for the Laser group. This indicates that there was no significant difference, tab. (2).

Table 1: Demographic data of included subjects

	Zone I ROP and APROP		P. Value	Zone II ROP		P. Value
	Anti-VEGF group (N = 78)	Laser (N = 32)		Anti-VEGF group (N = 104)	Laser (N = 56)	
Sex						
▪ Male	42 (53.85%)	14 (43.75%)	0.33	54 (51.92%)	29 (51.79%)	0.987
▪ Female	36 (46.15%)	18 (56.25%)		50 (48.08%)	27 (48.21%)	
GA (Weeks)	29.55 ± 1.71	29.59 ± 1.69	0.9	28.86 ± 1.47	30.45 ± 1.69	<0.0001*
Birth Weight (g)	1344.08 ± 194.44	1372.75 ± 204.17	0.5	1290.44 ± 269.83	1453.2 ± 279.04	<0.0001*
Follow up (Months)	17.27 ± 3.83	17.14 ± 3.23	0.87	18.79 ± 8.22	24.89 ± 13.18	<0.0001*

Table 2: The comparison of efficacies and treatment outcomes

	Zone I ROP and APROP		P. Value	Zone II ROP		P. Value
	Anti-VEGF group (N = 78)	Laser (N = 32)		Anti-VEGF group (N = 104)	Laser (N = 56)	
Initial regression	65 (83.33%)	20 (62.5%)	0.0179*	101 (97.13%)	55 (98.21%)	0.6711
Reactivation	22 (28.2%)	14 (43.75%)	0.1145	20 (19.23%)	3 (5.36%)	0.017*
Retinal detachment	4 (5.13%)	5 (15.63%)	0.0681	1 (0.96%)	1 (1.79%)	0.6545

4. Discussion

Due to the emergence of anti-VEGF medications, the usage of laser therapy in the treatment of retinopathy of prematurity (ROP) has significantly decreased. This is a significant improvement. In contrast, laser therapy continues to be the treatment of choice at our institution for patients who reside in remote areas or who have trouble traveling to numerous follow-up consultations. This is because laser therapy is able to target specific areas of the body. The parents of children who had been diagnosed with ROP were involved in a significant amount of discussion with the medical staff. The anti-VEGF medication was selected by the majority of the parents since it is simple to administer, does not cause any ill effects, and is quite effective. Furthermore, persons who are unable to endure general anesthesia and have retinopathy of prematurity (ROP) are the only individuals who have the choice of utilizing anti-VEGF medicine as an alternate treatment option. According to the findings of our cohort research, persons who were diagnosed with Zone II ROP and received anti-VEGF treatment had lower gestational ages, birth weights, and postmenstrual ages than those who received laser therapy. This was the case regardless of whether or not they received laser therapy. Rather of administering anti-VEGF injections, laser therapy was chosen as the most effective treatment option in the event that cases of retinopathy of prematurity (ROP) were discovered. ROP was characterized by the development of fibrous tissue on the ridge of the eye. The conclusion that anti-VEGF injections have the potential to worsen retinal traction and raise the probability of retinal detachment is the basis for this choice. This is especially true in situations where there is fibrotic proliferation. The foundation for this choice is as follows. It is probable that this occurrence is associated to the effect that anti-VEGF drugs have on the control of fibrotic processes, which in turn influences the decisions that are made

about the continuation of therapy. The size of the avascular zone, which indicates the location of the posterior lesion, was utilized to direct further treatment operations in cases with retinopathy of prematurity (ROP) that had returned after the initial injectable therapy had been administered. It was necessary to take these steps in order to guarantee that the appropriate therapy was delivered. In order to reduce the likelihood of suffering substantial visual field abnormalities, it was suggested that anti-VEGF drugs be employed rather than laser therapy. This was done in order to lower the likelihood of experiencing these abnormalities. When, on the other hand, retinopathy of prematurity (ROP) resurfaced despite the existence of a significant avascular zone and after two injections had been delivered, laser therapy was utilized. This was done in order to address the condition. According to the findings of our clinical research, anti-VEGF drugs and laser treatment are just as successful as solo therapies when it comes to the management of type 1 ROP and aggressive posterior ROP. Through the course of our investigation, we were able to establish this. In the event that these therapies are applied in combination with one another, a comprehensive strategy is established for the purpose of tackling the numerous obstacles that are brought about by this condition. It has been demonstrated that anti-VEGF drugs are useful in the treatment of zone I type 1 retinopathy of prematurity (ROP) as well as aggressive posterior ROP (A-ROP). Additionally, Linghu et al. [8] found that anti-VEGF drugs had a higher incidence of early regression (86%) in zone I ROP and aggressive ROP (A-ROP) when compared to laser ablation (71%) ($P < 0.001$). This finding is in agreement with our own findings. This suggests that anti-VEGF medicines could be a more efficient way to regulate the illness than other methods. It is conceivable that the lower first regression rate that was reported in these zones following laser therapy was the result of technical issues that were linked

with the process. These issues led to insufficient treatment and delayed disease management, which ultimately contributed to the lower rate of initial regression. For example, when compared to laser therapy, which was responsible for 22% of instances of retinal detachment, the use of anti-VEGF medicine resulted in a substantial reduction of 10% in the occurrence of retinal detachment ($P=0.001$). This demonstrates that the treatment is effective in arresting the advancement of the condition. In addition, it is important to point out that the reactivation rate of 47% was seen in eyes that were treated with anti-VEGF medications. The rate of reactivation was observed to be significantly reduced when compared to the reactivation rate of 66% of eyes that were treated with laser ablation ($P<0.001$). When it comes to the initial regression, advancement of retinal detachment, and rates of reactivation, anti-VEGF medications appear to be more useful than laser therapy for zone I ROP and A-ROP. Laser therapy is one of the treatments that is used for these conditions. The findings of past study, which are in agreement with current findings, lend weight to this assertion. Our findings provide validity to the findings of previous studies that shown the effectiveness of anti-VEGF drugs in the treatment of ROP syndrome. These studies were conducted in the past. The research that was conducted by Vedantham et al. [9] covered the assessment of forty-six eyes that had been diagnosed with retinopathy of prematurity (ROP) and had been treated with anti-VEGF drugs. The eyes had been examined in order to determine the severity of the condition. The study effort, which was of a retrospective nature, contained a case series as one of its components. Every single patient who was diagnosed with ROP saw a complete remission of the ailment after a week of making use of the drug. Researchers Bai et al. [10] did a study in which they studied the efficacy of intravitreal injection of conbercept (IVC) in the treatment of eyes that were afflicted by either aggres-

sive posterior retinopathy of prematurity (APROP) or Type 1 retinopathy of prematurity (ROP). The study was published in the journal *Clinical and Translational Medical Research*. Although there was a recurrence rate of 16.7%, all of the eyes that were treated showed full remission of ROP. This was the case after the treatment was administered. It is compatible with the findings of previous studies, such as the one that was carried out by Mintz-Hittner et al. [11], which shown that anti-VEGF drugs led to reduced reactivation rates in contrast to laser therapy. The recurrence rate is consistent with these findings. Laser photocoagulation and anti-VEGF drug treatment have both shown comparable degrees of effectiveness when it comes to treating eyes that have zone II retinopathy of prematurity (ROP). Both of these treatments have been done successfully. Laser therapy, on the other hand, has been shown to provide a much-decreased risk of reactivation when compared to anti-VEGF treatment. Linghu et al. [8] found that significant rates of initial regression were reported in both the anti-VEGF and laser therapy groups for zone II ROP. The rates of regression found in the laser treatment cohort were 99% and 99 percent, respectively. When compared to the rates that were seen in zone I and aggressive ROP (A-ROP), which were 85% and 71% respectively, these rates were considerably higher. These findings are consistent with the data that we have obtained. $P=0.406$ indicates that there was not a difference between the two treatment groups that could be regarded to be statistically significant. The incidence of retinal detachment was found to be relatively low, with rates of 0.8% for anti-VEGF treatment and 1.1% for laser treatment, and a p-value of 0.136. This was demonstrated by the findings of the study. However, the incidence of reactivation was significantly greater with anti-VEGF therapy, which was 21%, in comparison to laser treatment, which was only 8% ($P=0.009$). This was the case despite the fact that the laser

treatment was only 8%. When contrasted to the findings of the BEAT-ROP research that was conducted by Mintz-Hittner et al. in 2011, which discovered reactivation rates of 5.1% and 11.2% for the two treatments, respectively, this specific discovery stands in striking contrast to the findings of that study on the subject of reactivation rates. Throughout the course of our investigation, we made a distinction between the reactivation criteria and the many types of ROP that were examined. One possible explanation for the reduced reactivation that was seen in the posterior area of retinopathy of prematurity (ROP) is that the greater difficulties that are connected with laser therapy in this particular site may be to blame. The consequences of retinopathy of prematurity (ROP) might be affected by factors such as ethnicity and variations in the population that is affected by the condition. This is a potential that exists. When compared to anti-VEGF treatment, laser therapy offers a more long-lasting eradication of aberrant blood vessels. This treatment results in less changes in the levels of vascular endothelial growth factor (VEGF), which in turn reduces the likelihood that the abnormal blood vessels would restart. For patients with stage 3+ zone II illness, intravitreal ranibizumab (IVR) had a greater rate of therapeutic effectiveness (88%) compared to laser therapy (70%) in terms of effective treatment. According to the findings of the zone I ROP research that Stahl et al. [12] conducted, this conclusion is in agreement with the findings. According to the findings of two studies conducted by Zhang et al. [13] and Karkhaneh et al. [14], which focused on zone II ROP, it was discovered that the use of intravitreal bevacizumab (IVB) or intravitreal ranibizumab (IVR) as the only therapy resulted in an increased likelihood of the illness returning. The regression of retinopathy of prematurity

(ROP) in these clinical trials needed further treatment in the form of a second intravitreal injection of bevacizumab (IVB) or ranibizumab (IVR), or laser therapy treatments. This was the case in the majority of the instances. Beginning with the initial injection and continuing through the retreatment, there were a number of different time periods that took place. According to the findings of our research, the reactivation rate of eyes that were treated with anti-VEGF medications was 21%, which was greater than the reactivation rate of 8% that was found in eyes that were treated with laser therapy for zone II ROP. Reactivation rates were higher in eyes that were treated with anti-VEGF medications. Anti-VEGF drugs exhibited a decreased risk of reactivation when compared to laser therapy for posterior zone II ROP, according to the BEAT-ROP investigation that was carried out in 2011 by Mintz-Hittner et al. [11] In contrast to the results of the BEAT-ROP experiment, this findings are not the same. Both the definition of reactivation and the distribution of the various kinds of ROP, as well as the characteristics of the population that was analyzed, can be related to the disparities in reactivation rates that were observed. Our definition of reactivation, in contrast to the BEAT-ROP research, placed a stronger focus on the existence of ridge recurrence or illness in conjunction to reactivation, rather than neovascularization. This was done in order to distinguish reactivation from any other condition. In addition, we included all instances of ROP that were classified as zone II and that met the diagnostic criteria for type 1 ROP. This stands in stark contrast to the findings of the BEAT-ROP study, which excluded participants with anterior zone II ROP from the study without exception.

5. Conclusion

Anti-VEGF therapy, notably Ranibizumab, outperforms laser photocoagulation for ROP treatment in aggressive forms in Zone I. This appears to show better initial regression, lesser reactivation, and lower retinal detachment. Anti-VEGF therapy, and laser photocoagulation for ROP treatment

in Zone II appears to show comparable initial regression and retinal detachment but laser show lesser reactivation than Anti-VEGF therapy.

References

1. Dogra, M., Katoch, D. & Dogra, M. An update on retinopathy of prematurity (ROP). *The Indian J. of Pediatrics*. 2017; 84: 930-936.
2. Moshfeghi, D. Systemic solutions in retinopathy of prematurity. *American J. of Ophthalmology*. 2018; 193: xiv-xviii.
3. Jaju, S., Patil, N., Gajra, B., et al. Evolution of classification and treatment of retinopathy of prematurity: A review article. *TNOA J. of Ophthalmic Science and Research*. 2023; 61 (3): 281-289.
4. Berrocal, A., Fan, K., Al-Khersan, H., et al. Retinopathy of prematurity: Advances in the screening and treatment of retinopathy of prematurity using a single center approach. *American J. of Ophthalmology*. 2022; 233: 189-215.
5. Mintz, H. Bevacizumab eliminates the angiogenic threat of retinopathy of prematurity (BEAT-ROP). *Clinical Trials*. 2010; 364 (7): 603-615.
6. Tran, K., Cernichiaro-Espinosa, L. & Berrocal, A. Management of retinopathy of prematurity-use of anti-VEGF therapy. *Asia-Pacific J. of Ophthalmology*. 2018; 7 (1): 56-62.
7. Bressler, N., Kaiser, P., Do, D., et al. Biosimilars of anti-vascular endothelial growth factor for ophthalmic diseases: A review. *Survey of Ophthalmology*. 2024; 69 (4): 521-538.
8. Linghu, D., Cheng, Y., Zhu, X., et al. Comparison of intravitreal anti-VEGF agents with laser photocoagulation for retinopathy of prematurity of 1,627 eyes in China. *Frontiers in Medicine*. 2022; 9: 911095.
9. Vedantham, V. Intravitreal aflibercept injection in Indian eyes with retinopathy of prematurity. *Indian J. of Ophthalmology*. 2019; 67 (6): 884-888.
10. Bai, Y., Nie, H., Wei, S., et al. Efficacy of intravitreal conbercept injection in the treatment of retinopathy of prematurity. *British J. of Ophthalmology*. 2019; 103 (4): 494-498.
11. Mintz-Hittner, H., Kennedy, K. & Chuang, A. Efficacy of intravitreal bevacizumab for stage 3+ retinopathy of prematurity. *New England J. of Medicine*. 2011; 364 (7): 603-615.
12. Stahl, A., Lepore, D., Fielder, A., et al. Ranibizumab versus laser therapy for the treatment of very low birth-weight infants with retinopathy of prematurity (RAINBOW): An open-label randomized controlled trial. *The Lancet*. 2019; 394 (10208): 1551-1559.
13. Zhang, G., Yang, M., Zeng, J., et al. Comparison of intravitreal injection of ranibizumab versus laser therapy for zone II treatment-requiring retinopathy of prematurity. *Retina*. 2017; 37 (4): 710-717.
14. Karkhaneh, R., Khodabande, A., Riazi-Eafahani, M., et al. Efficacy of intravitreal bevacizumab for zone-II retinopathy of prematurity. *Acta Ophthalmologica*. 2016; 94 (6): e417-e420.