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Early avastin (Bevacizumab) Administration for acute retinal vein occlusion: A key strategy for improved patient outcomes.

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ABSTRACT… Objective: To find the mean change in BCVA and CMT after intravitreal injection Avastin administration in patients with acute retinal vein occlusion with macular edema. **Study Design:** Quasi-experimental study. **Setting:** LRBT Eye Hospital, Lahore. **Period:** October 2024 to March 2025.. **Methods:** 60 Patients with acute retinal vein occlusion (RVO) and macular edema, diagnosed within three months of symptom onset. Patients received monthly intravitreal injections of bevacizumab (1.25 mg in 0.05 mL) over three months. Bevacizumab, a widely used anti-VEGF agent, is known to reduce macular swelling and improve vision. The primary outcomes were changes in best-corrected visual acuity (BCVA, logMAR) and central macular thickness (CMT, μm), reflecting vision clarity and macular edema, respectively. Both were monitored using high-resolution optical coherence tomography (OCT), a non-invasive imaging modality. Baseline characteristics were analyzed to assess correlations between demographics, disease duration, and treatment response. **Results:** The study demonstrated significant improvements: mean baseline BCVA improved from 1.09 ± 0.17 to 0.56 ± 0.19 ($p < 0.001$), and mean CMT decreased from 455.48 ± 52.05 μm to 300.66 ± 63.96 μm ($p < 0.001$) after three months. No systemic or ocular adverse events were recorded, supporting bevacizumab's efficacy and safety for RVO-associated macular edema. **Conclusion:** We found Intravitreal bevacizumab is a safe and effective method of treatment while dealing with macular edema secondary to RVO in our population, providing significant improvements in VA and MT.

Key words: BCVA, CMT, Intravitreal Bevacizumab, Macular Edema, RVO.

INTRODUCTION

The condition known as retinal vein occlusion (RVO) is quite common and is the second leading cause of vascular disorders that threaten vision, after diabetic retinopathy. The incidence of central retinal vein occlusion (CRVO) is currently estimated at 1.8%.[1]1988-1990 Prevalence rates also vary by region and demographic characteristics, with higher rates observed in older populations and certain ethnic groups. However, a limited number of studies have explored these regional and racial disparities, underscoring the need for more geographically diverse research. However, the treatment of macular edema associated with this condition remains controversial and challenging. Although both surgical and medical approaches have been explored, no clear consensus exists regarding treatment guidelines or modalities, particularly following the branch vein occlusion (BVO) and central vein occlusion (CVO) studies.[2] RVOs lead to decreased tissue perfusion and increased hydrostatic pressure, which results in macular edema, intraretinal hemorrhages, varying levels of ischemia, fluid exudation, wrinkling retinopathy, and the possible development of ocular neovascular complications.[3]

Several therapeutic methods are used to treat macular edema caused by branch retinal vein occlusion (BRVO).[4] These include the use of anti-VEGF injections, which directly target the excessive vascular permeability contributing to the edema, and corticosteroid therapies that help reduce inflammation and vascular leakage. Laser photocoagulation is another modality, particularly useful for stabilizing chronic cases or when

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pharmacological treatments are unavailable. Combination therapy, using both pharmacological and laser treatments, is also being explored for more complex or refractory cases.[5]

Macular grid laser photocoagulation was initially recommended following the Branch Vein Occlusion Study (BVOS); however, subsequent studies indicated that its improvement in visual function was limited.[6]presence of macular edema and angiographic features were recorded during the follow-up period. Results: Visual acuity increased significantly in both groups after 3 months of follow-up ($p<0.001$ The CVO study, however, found no advantage of macular grid laser treatment for cystoid macular edema (CME) caused by CRVO. To address this, researchers have turned their focus to other methods, which include laser-induced chorioretinal anastomosis, arteriovenous sheathotomy, intravitreal tissue plasminogen activator, radial optic neurotomy, and therapeutic options like intravitreal steroids or anti-VEGF agents, such as Pegaptanib sodium (Macugen), Ranibizumab (Lucentis), and Bevacizumab (Avastin).[7]

Despite their efficacy, anti-VEGF therapies pose challenges, including increased risk of cataract formation and elevated intraocular pressure, particularly with frequent injections. Additionally, the financial burden of continuous treatment and limited long-term data complicate patient management.[8]

Elevated vascular endothelial growth factor (VEGF) levels are central to the pathophysiology of retinal vein occlusions (RVOs), causing complications like macular edema, ischemia, and neovascularization. Anti-VEGF therapies have become a cornerstone in managing these issues by directly targeting VEGF-driven vascular permeability and inflammation.[9] Intravitreal bevacizumab (Avastin, Genentech, Inc., San Francisco, CA), a recombinant monoclonal antibody that targets VEGF, has shown efficacy in reducing macular edoema in eyes impacted by RVOs.[10] Inhibiting VEGF with bevacizumab injections has become a dependable alternative therapy for macular edoema linked to RVOs. Short-term studies on intravitreal Avastin (IVA) reveal great improvements in VA and MT, highlighting VEGF's critical role in RVO pathogenesis. Yet, the scarcity of long-term outcome data necessitates ongoing research to evaluate its sustained benefits and potential risks.[11]

METHODS

This study adopted a quasi-experimental design and was conducted at LRBT (Layton Rahmatulla Benevolent Trust) Eye Hospital on Multan Road, Lahore. The study duration spanned six months (October 2024 to March 2025) following the approval from the Ethical Committee (Reference No: Co/Admin/Doc-251).

The sample size was calculated as 60 patients with retinal vein occlusion. It was determined using a 95% confidence level, absolute precision (d) = 0.03, and a mean change in BCVA of 0.52 ± 0.09. The selected cases included patients with retinal vein occlusion (RVO) enrolled through non-probability consecutive sampling. The study population comprised patients aged 18 to 65 years who presented with acute RVO (CRVO or BRVO) of less than three months' duration and associated macular edema, with no prior treatment for RVO.

Formal approval from the hospital's ethical committee was obtained before initiating the study, and informed written consent was collected from all participants. Privacy and confidentiality were maintained in compliance with the Helsinki Declaration of Bioethics. At LRBT Eye Hospital, strict adherence to aseptic techniques ensured the safe administration of intravitreal injections. Potential risks such as endophthalmitis and elevated intraocular pressure were mitigated through a comprehensive post-injection follow-up protocol. A pretested proforma was used to collect data, which included a detailed evaluation performed by the researcher. The initial assessment involved Snellen visual acuity testing, IOP measurement with applanation tonometry, slit-lamp examination of the anterior and posterior segments using Volk lenses (90 and 78 diopters), and optical coherence tomography (OCT) for central macular thickness (CMT) measurement.

For all patients, baseline CMT and BCVA readings were evaluated and recorded on proforma.

Intravitreal Avastin injections were administered following the hospital protocol in an aseptic operating theater environment. The procedure involved preparing the eyelids and conjunctiva with povidone iodine (10% for the lids and 5% for the conjunctiva, instilled three times several minutes apart). Bevacizumab (Avastin) was injected at a dose of 1.25 mg in 0.05 ml via the pars plana, 3.5–4.0 mm from the surgical limbus. After the injection, antibiotic eye drops were applied, and the eye was dressed with a sterile cotton pad. Follow-up evaluations were scheduled for the next day, at one week, and monthly for three months, during which OCT and clinical examinations were repeated. Treatment outcomes were determined based on the mean change in BCVA and CMT. Non-improving patients or those with recurrent macular edema were considered for additional injections during the study.

In the event of complications, patients were provided with immediate treatment at no additional cost. This approach aligns with LRBT's mission to deliver high-quality care in a resource-limited setting, demonstrating its commitment to patient safety. Data collected during the study were entered into SPSS software (version 25.0) for analysis. Quantitative variables such as age, baseline and post-treatment CMT and BCVA, and their changes were expressed as mean and standard deviation. Gender and other qualitative variables were summarized as frequencies and percentages. Changes in CMT and BCVA pre- and post-treatment were analyzed using paired sample t-tests, with stratification based on age, gender, and disease duration. A p-value of less than 0.05 was deemed statistically significant.

RESULTS

A detailed summary of the demographic and clinical characteristics of the 60 study participants is presented in Table-I. The age distribution indicates that 35% of the participants are between 18 and 50 years old, while 65% fall into the 51–65 age bracket. The mean age of the participants is 41.00 ± 13.72 years, suggesting that this condition is more prevalent among older adults. The gender breakdown shows that 41.7% of the participants are males (n=25) and 58.3% are females (n=35), demonstrating a mild female predominance. Moreover, the duration of retinal vein occlusion in this cohort averages 6.67 ± 3.40 weeks, highlighting its acute presentation. These findings contribute valuable context to the understanding of the population affected by this condition and form a basis for further analysis.

Table-II provides an in-depth analysis of the therapeutic impact of intravitreal Avastin injections on best-corrected visual acuity (BCVA) and central macular thickness (CMT) in patients with acute retinal vein occlusion (RVO) and macular edema. At baseline, the mean BCVA of the study cohort was 1.09 ± 0.17 logMAR, indicative of significant visual impairment caused by the condition. After three months of monthly intravitreal Avastin injections, BCVA showed a substantial improvement, with the mean value decreasing to 0.56 ± 0.19 logMAR, representing a mean change of 0.53 ± 0.09 logMAR. This improvement, both statistically significant ($t = 43.121$, $p < 0.001$) and clinically meaningful, underscores Avastin's efficacy in restoring visual function. By halving the visual deficit, Avastin enables patients to regain functional vision, significantly improving their quality of life and ability to perform daily tasks.

The improvement in BCVA reflects Avastin's mechanism of action as an anti-VEGF agent, which reduces vascular permeability, alleviates edema, and restores the structural integrity of the retina. This finding aligns with the global clinical experience with Avastin, where similar outcomes have been reported, such as in studies by Mehany et al. and Gutiérrez et al. These studies similarly demonstrated marked improvements in BCVA, validating Avastin's effectiveness across different populations.

Equally significant were the anatomical improvements observed in central macular thickness (CMT). At baseline, the mean CMT was 455.48 ± 52.05 μm, reflecting pronounced macular edema. Following treatment, the

mean CMT decreased to 300.66 ± 63.96 μm, corresponding to a mean reduction of 154.83 ± 29.80 μm. This reduction was highly statistically significant ($t = 40.244$, $p < 0.001$) and demonstrated the resolution of macular edema to near-normal levels. The decrease in CMT directly correlates with improved photoreceptor function, which is critical for visual acuity. These findings further validate Avastin's role in reducing macular swelling and improving anatomical outcomes.

The concurrent improvements in BCVA and CMT highlight Avastin's dual efficacy in providing both functional and anatomical benefits. The study outcomes are consistent with international research, including studies by Thapa et al., which demonstrated similar reductions in CMT and visual improvements over more extended periods. While the current study focused on a 3-month follow-up, the results provide a strong foundation for future research exploring Avastin's long-term effects and potential for sustained benefits in managing macular edema secondary to RVO.

Variable	Group	Frequency	Percent
Age(years)	18-50	21	35.0
	51-65	39	65.0
	Mean+SD	47.80+16.58	
Gender	Male	25	41.7
	Female	35	58.3
Duration of Retinal Vein Occlusion (weeks)	**Mean+SD**	6.67+3.40	

Table-I. Characteristics of participants: demographic and clinical (N=60)

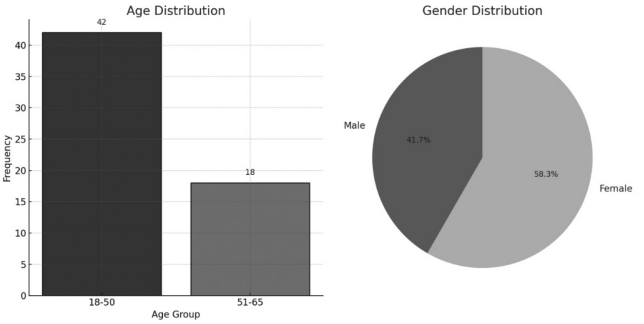

Figure-1

DISCUSSION

Our study demonstrated significant improvements in BCVA and CMT following intravitreal bevacizumab (Avastin) therapy in cases with ME secondary to RVO. These results align with international studies, such as those by Lobo and co- authors[13], and Gutiérrez co-workers[14], who also reported substantial functional and anatomical benefits from intravitreal bevacizumab injections. However, our study fills a critical gap by addressing the treatment outcomes in our population, where limited data on this subject exist.

When considering age and gender distributions, a local study examining patients undergoing green laser therapy reported that out of 2,058 patients, 86 (4.18%) were diagnosed with RVO. Among these, 54.65% were female, and 45.35% were male, indicating a mild female predominance. This gender trend is comparable to our cohort, where females also constituted a larger proportion of the study population (58.3%).

Variable		Mean	Std. Deviation	95% CI Lower	95% CI Upper	t-value	P-Value
VA	Baseline	1.09	0.17	0.50	0.55	43.121	0.000
	Follow-up	0.56	0.19				
	Change	0.53	0.09				
CMT	Baseline	455.48	52.05	147.13	162.52	40.244	0.000
	Follow-up	300.66	63.96				
	Change	154.83	29.80				

Table-II. Mean improvement in BCVA and reduction in CMT after avastin injection in acute retinal vein occlusion patients with macular edema

The local study also revealed that 76.74% of RVO cases occurred in individuals over 40 years of age, reflecting the age-related nature of vascular pathologies. This observation parallels the findings of our study, where the mean age of participants was 47.80+16.58 years, further corroborating the demographic characteristics commonly associated with RVO.[15]

In our study, the mean change in BCVA (from 1.09 ± 0.17 to 0.56 ± 0.19 logMAR) and CMT (from 455.48 ± 52.05 μm to 300.66 ± 63.96 μm) closely mirrors the outcomes observed by Mehany et al[20] (logMAR improvement from 1.08 ± 0.52 to 0.48 ± 0.32 and CMT reduction from 455 ± 126 μm to 250 ± 48 μm). Similarly, Lobo et al[13] and Gutiérrez et al[14] reported comparable improvements in BCVA and CMT, emphasizing the global efficacy of bevacizumab therapy.

Gutiérrez and others, in a study revealed the mean visual acuity (VA) improved significantly from 1.32 ± 0.24 logMAR at baseline to 0.52 ± 0.09 at the 6-month follow-up ($p = 0.0003$), with a mean change of 0.52 ± 0.09. The macular edema showed a prompt response, with a trend toward restoration of normal macular anatomy as early as the seventh day. Additionally, foveal thickness reduced significantly from 615.50 ± 116.29 μm to 195.5 ± 43.7 μm ($p = 0.001$), and macular volume decreased from 19.81 ± 2.31 mm^3 to 9.23 ± 1.38 mm^3 ($p = 0.0001$), indicating substantial anatomical improvement.[14]

Interestingly, our findings also align with those of Thapa et al[16] in Nepal, where the mean CMT improved from 515.3 ± 189.4 μm to 233.6 ± 101.5 μm at 12 months. This similarity in outcomes highlights the consistent therapeutic potential of bevacizumab across diverse populations and geographic regions, despite differences in healthcare systems, patient demographics, and socioeconomic conditions.

In our country, the Avastin is a cost-effective alternative to other anti-VEGF agents like ranibizumab (Lucentis) and aflibercept (Eylea). Given the financial constraints of the majority of the population, bevacizumab offers a viable treatment option. However, challenges such as unregulated drug pricing and inconsistent availability may impact its widespread use. Most tertiary eye care centers in our country, including LRBT, have the facilities to administer intravitreal injections safely. However, patients in rural areas face difficulties accessing such specialized services, resulting in delayed diagnoses and treatment. This delay may lead to irreversible vision loss, as seen in patients presenting with chronic or ischemic RVO.

In our country, diabetes is a substantial risk factor for reactive oxygen species (RVO). Kabunga et al.'s[17] research highlighted superior results in individuals with diabetic macular oedema (DME), which fits with our observation of favourable responses in patients with systemic comorbidities. The study conducted by Kabunga et al[17] highlights the need of integrating diabetes and ophthalmology clinics in order to handle both systemic and ocular problems simultaneously.

According to the results of earlier studies, such as those conducted by Gutiérrez et al[14] and Kabunga et al[17] our research confirmed that there were no adverse events that occurred in the systemic or ocular domains. However, it is still very important to carefully monitor for complications such as endophthalmitis and elevated intraocular pressure, particularly in environments with less stringent aseptic measures.

The short follow-up duration of three months restricts our ability to evaluate the long-term effects of bevacizumab, despite its proven efficacy in this study. Previous research, such as that by Thapa et al[25] and Noma et al., suggests that follow-up over at least one year is essential to determine the recurrence of macular edema and the sustainability of visual improvements.

Conducted at LRBT Eye Hospital, the study's single-center design limits its generalizability to other regions of Pakistan, particularly rural areas where healthcare access is limited. Non-probability consecutive sampling may have introduced selection bias, while the exclusion of chronic retinal vein occlusion cases limits the scope to acute conditions. Additionally, the study

did not evaluate adverse effects extensively, and the lack of stratification by systemic comorbidities, such as diabetes and hypertension, leaves gaps in understanding their impact on treatment outcomes. To optimize care for RVO patients in Pakistan, standardized treatment protocols, government subsidies for anti-VEGF therapy, and enhanced ophthalmologist training are essential to ensure safe, effective, and equitable care.

CONCLUSION

Intravitreal bevacizumab is a safe, cost-effective, and efficacious option for managing macular edema secondary to RVO in the Pakistani population. By addressing systemic comorbidities, improving healthcare access, and enhancing patient education, we can further maximize the benefits of this treatment and reduce the burden of vision-threatening complications in our population.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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1	**Aamna Iqbal:** Data collection, paper writing.
2	**Sidra Zafar:** Review of manuscript.
3	**Hassam Mukhtar:** Data collection, analysis, paper writing.
4	**Zukhruf Ijaz:** Discussion writing, review of manuscript.
5	**Talha Nafees:** Literature, review and data entry.
6	**Farhan Ali:** Data analysis, review of manuscript.