ONLINE ISSN :3007-309X
PRINT ISSN :3007-3081

Journal of Medical & Health Sciences Review

EVALUATION OF VISUAL AND ANATOMICAL OUTCOMES AFTER INTRA-VITREAL ANTI-VASCULAR ENDOTHELIAL GROWTH FACTOR INJECTION IN PATIENTS WITH DIABETIC DIFFUSE MACULAR EDEMA

Dr. Ahmad Hassan[1], Dr. Aleem Hamza Bajwa[2], Dr. Muhammad Kashif Bilal[3]

[1]MBBS, Post Graduate Trainee, Department of Ophthalmology, Bahawal Victoria Hospital Bahawalpur, Email: aahmadhasssan@yahoo.com
[2]MBBS, Medical Officer, BHU Rajar Hoo, Email: bajwa.aleem443@gmail.com
[3]MBBS, Medical Officer, BHU Chak Himta. Email: mkb.kpr710@gmail.com

ARTICLE INFO:
Keywords:
Diabetic Macular Edema (DME), Anti-VEGF Therapy, Intravitreal Injections

Corresponding Author:
Dr. Ahmad Hassan
MBBS, Post Graduate Trainee, Department of Ophthalmology, Bahawal Victoria Hospital Bahawalpur, Email: aahmadhasssan@yahoo.com

Article History:
Published on 04 July 2025

ABSTRACT

Aim: This study aimed to evaluate the visual and anatomical outcomes following intravitreal anti-vascular endothelial growth factor (anti-VEGF) injections in patients with diffuse diabetic macular edema (DME). The primary objective was to assess improvement in best-corrected visual acuity (BCVA) and reduction in central retinal thickness (CRT) as measured by spectral domain optical coherence tomography (OCT).

Methods: A descriptive cross-sectional study was conducted at the Ophthalmology Department of Bahawal Victoria Hospital, Bahawalpur, over a six-month period. A total of 147 treatment-naïve patients aged 20–60 years with type 2 diabetes and diffuse DME confirmed by OCT (CRT ≥290 µm) were included. Participants received three monthly intravitreal anti-VEGF injections (bevacizumab, ranibizumab, or aflibercept). Visual acuity was assessed using Snellen's chart and CRT was measured via OCT before treatment and two weeks after the third injection. The primary endpoint was defined as achieving both BCVA ≥20/40 and CRT ≤290 µm post-treatment. Secondary endpoints included changes in BCVA (in Snellen lines) and CRT (in micrometers). Data were analyzed using SPSS version 25.0.

Results: Following three intravitreal anti-VEGF injections, there was a statistically significant improvement in both visual and anatomical outcomes. The proportion of patients achieving BCVA ≥20/40 increased from 12.2% pre-treatment to 48.3% post-treatment

($p < 0.001$), with a mean gain of 3.2 ± 1.5 Snellen lines. Mean CRT decreased significantly from 410.5 ± 45.6 µm at baseline to 287.3 ± 32.4 µm post-treatment ($p < 0.001$), with 65.3% of patients achieving CRT ≤290 µm. A combined outcome of improved BCVA and reduced CRT was achieved in 42.2% of patients. No major adverse events were reported, and transient intraocular pressure spikes occurred in 5% of cases.

Conclusion: Intravitreal anti-VEGF therapy is effective in improving both visual acuity and reducing macular thickness in patients with diffuse diabetic macular edema. Early response to treatment, as assessed by OCT, can guide further management. While most patients benefit from anti-VEGF therapy, approximately 40% show partial or no improvement, highlighting the need for early identification of non-responders and consideration of alternative treatment strategies. Regular OCT monitoring and individualized treatment approaches are essential for optimizing long-term outcomes in patients with DME.

INTRODUCTION

Diabetic retinopathy (DR) is a leading cause of preventable blindness worldwide, with diabetic macular edema (DME) being the primary cause of vision loss among affected individuals [1]. DME results from increased vascular permeability due to chronic hyperglycemia-induced retinal damage, which leads to fluid accumulation in the macula [4]. Studies have shown that approximately 27% of patients with type 1 diabetes develop macular edema within 9 years of disease onset, while in type 2 diabetes, the prevalence increases from 3% within 5 years to 28% after 20 years [2,3].

Anti-VEGF agents such as ranibizumab, aflibercept, and bevacizumab have emerged as first-line therapies for center-involved DME due to their ability to reduce vascular permeability and improve visual acuity [5,6]. Clinical trials, including those by the Diabetic Retinopathy Clinical Research Network (DRCR.net), have demonstrated significant improvements in visual acuity and reductions in central subfield thickness (CST) following anti-VEGF treatment [13,14]. However, approximately 40% of patients show suboptimal response to these agents, highlighting the need for early identification of non-responders and alternative treatment strategies [7,8].

Optical coherence tomography (OCT) has become an essential tool for diagnosing and monitoring DME, providing detailed structural information on retinal layers and enabling quantitative assessment of macular thickness [9]. Early changes in OCT parameters after anti-VEGF treatment may serve as predictive biomarkers for long-term outcomes [11].

This study evaluates the visual and anatomical outcomes of intravitreal anti-VEGF therapy in patients with diffuse DME using OCT-based criteria and aims to contribute to the growing body of evidence supporting its use in clinical practice.

MATERIALS AND METHODS

A descriptive cross-sectional study was conducted at the Ophthalmology Department of Bahawal Victoria Hospital, Bahawalpur. The study duration was six months, and ethical approval was obtained from the hospital's research and ethics committee and CPSP. Using WHO sample size calculation

and assuming a 45.5% improvement rate in BCVA with a 95% confidence level and 8% margin of error, a sample size of 147 patients was calculated. Non-probability consecutive sampling was used to enroll eligible participants. This study included a total of 147 patients diagnosed with type 2 diabetes mellitus who presented with diffuse diabetic macular edema (DME) confirmed by optical coherence tomography (OCT). Participants were aged between 20 and 60 years and were of both genders. All patients had central macular thickness (CMT) greater than or equal to 290 µm on OCT, which is consistent with diffuse DME. Visual acuity at baseline was either worse than 6/18 or better than 6/12. Both eyes of the patients could be included in the analysis if they met the inclusion criteria. Patients were treatment-naïve for any prior intravitreal anti-vascular endothelial growth factor (anti-VEGF) or corticosteroid injections and had not undergone recent laser photocoagulation or vitreoretinal surgery. Patients were excluded from the study if they had focal macular edema caused solely by microaneurysmal leakage rather than diffuse retinal thickening. Those with hazy corneas that could interfere with accurate OCT imaging or visual acuity testing were also excluded. Additionally, individuals with other concurrent macular pathologies such as age-related macular degeneration (AMD), retinal vein occlusion, or any condition causing macular edema unrelated to diabetes were not included. Patients who had previously received panretinal photocoagulation (PRP) or grid laser treatment within the past six months were excluded to avoid confounding effects on visual and anatomical outcomes. Individuals with evidence of ischemic maculopathy, characterized by widening or irregularity of the foveal avascular zone on angiography, were also excluded due to the different management strategies required for this condition. Other exclusion criteria included the presence of high myopia, uveitis, macular holes, or any coexisting systemic conditions such as hypertension or chronic kidney disease (CKD), which might influence the progression of retinopathy or treatment response. Patients already receiving treatment for macular edema with anti-VEGF agents or corticosteroids were also excluded to ensure uniformity in treatment exposure across all participants.

Patients underwent baseline assessments including demographic data, medical history, visual acuity using Snellen's chart, and OCT to measure central retinal thickness. Three intravitreal anti-VEGF injections (bevacizumab, ranibizumab, or aflibercept) were administered four weeks apart. Two weeks after the third injection, visual acuity and OCT were repeated to assess outcomes.

Continuous variables (BCVA, CST, HbA1c, duration of diabetes, number of injections) and categorical variables (gender, diabetic retinopathy severity, hypertension, CKD, smoking) were analyzed using SPSS version 25.0. Data were expressed as mean ± SD for continuous variables and frequency (%) for categorical variables. A p-value < 0.05 was considered statistically significant.

RESULTS

A total of 147 patients diagnosed with type 2 diabetes and diffuse diabetic macular edema (DME) were included in this study. The mean age of the participants was 52.3 ± 7.8 years, with 54.4% males and 45.6% females. The average duration of diabetes was 8.6 ± 3.2 years, and the mean HbA1c level was 8.3 ± 1.1%. Baseline best-corrected visual acuity (BCVA) was worse than 6/18 in 62% of patients, indicating significant visual impairment before treatment.

All patients received three monthly intravitreal anti-VEGF injections, and outcomes were assessed two weeks after the third injection using Snellen's chart for BCVA and optical coherence tomography (OCT) for central retinal thickness (CRT). There was a statistically significant improvement in both functional and anatomical outcomes following treatment.

The proportion of patients achieving a BCVA of ≥20/40 increased from 12% at baseline to 48% post-treatment ($p < 0.001$). On average, patients gained 3.2 ± 1.5 lines of visual acuity on the Snellen chart. Among all participants, 89 patients (60.5%) showed improvement in visual acuity, while 58 patients (39.5%) had no change or minimal improvement.

Table 1: Visual Acuity Improvement After Anti-VEGF Injection

Parameter	Pre-Treatment	Post-Treatment	p-value
Number of Patients with BCVA ≥20/40	18 (12.2%)	71 (48.3%)	<0.001
Mean Snellen Lines Gained	-	3.2 ± 1.5	<0.001

Central retinal thickness, as measured by OCT, showed a marked reduction following anti-VEGF therapy. The mean central subfield thickness (CST) decreased from 410.5 ± 45.6 µm at baseline to 287.3 ± 32.4 µm post-treatment ($p < 0.001$). This corresponds to an average reduction of 123.2 µm. A total of 96 patients (65.3%) achieved a final CRT ≤290 µm, which is considered anatomical resolution of macular edema.

Table 2: Central Retinal Thickness Reduction After Anti-VEGF Injection

Parameter	Pre-Treatment	Post-Treatment	p-value
Mean CST (µm)	410.5 ± 45.6	287.3 ± 32.4	<0.001
Patients with CRT ≤290 µm	0	96 (65.3%)	<0.001

Of the 147 patients, 62 (42.2%) met the combined endpoint of improved BCVA (≥20/40) and reduced CRT (≤290 µm). Another 51 patients (34.7%) showed partial improvement—either in visual acuity or retinal thickness but not both. The remaining 34 patients (23.1%) had no significant improvement in either parameter.

Table 3: Combined Functional and Anatomical Outcomes

Outcome Category	Number of Patients	Percentage (%)
Achieved Both Criteria (BCVA≤20/40 + CRT <290 µm)	62	42.20%
Partial Response (Either BCVA or CRT improved)	51	34.70%
No Improvement	34	23.10%

In terms of safety, no major adverse events such as endophthalmitis, retinal detachment, or systemic thromboembolic events were reported during the follow-up period. Transient intraocular pressure spikes and mild anterior chamber inflammation were observed in 5% of cases, but these resolved spontaneously without additional intervention.

DISCUSSION

The findings of this study demonstrate that intravitreal anti-vascular endothelial growth factor (anti-VEGF) therapy significantly improves both visual and anatomical outcomes in patients with diffuse diabetic macular edema (DME). These results are consistent with recent clinical trials and real-world studies conducted within the last five years, reinforcing the role of anti-VEGF agents as first-line therapy for DME.

In our study, 48.3% of patients achieved a best-corrected visual acuity (BCVA) of ≥20/40 after three monthly anti-VEGF injections, with an average gain of 3.2 Snellen lines. This improvement aligns with data from the Diabetic Retinopathy Clinical Research Network (DRCR.net) Protocol V and Protocol A13, which reported mean BCVA gains of approximately 10–13 letters after one year of anti-VEGF therapy [13,14]. Although our follow-up period was shorter (only two weeks after the third injection), the observed improvements suggest that early response to treatment is predictive of long-term visual gains, as previously reported in post hoc analyses of clinical trial data [11].

Anatomically, we observed a significant reduction in central retinal thickness (CRT) from a baseline mean of 410.5 µm to 287.3 µm post-treatment, with 65.3% of patients achieving CRT ≤290 µm. This level of anatomical resolution is comparable to that seen in large prospective trials such as VISTA and VIVID, where aflibercept demonstrated CRT reductions from 400–450 µm to below 300 µm after 6–12 months of treatment [19]. Similarly, real-world studies have shown CRT reductions of 100–150 µm in more than 60% of treated eyes [17,18], further supporting the efficacy of anti-VEGF therapy even in heterogeneous clinical populations.

Interestingly, 42.2% of patients in our cohort achieved both functional (≥20/40 BCVA) and anatomical (CRT ≤290 µm) success. This dual outcome is critical, as not all patients who show anatomical improvement experience corresponding visual gains, and vice versa. Our result is slightly lower than the 50–60% combined success rates reported in some randomized controlled trials [13,16], which may be attributed to differences in patient selection criteria, baseline severity, and follow-up duration. Our inclusion of treatment-naïve patients with moderate-to-severe baseline CRT likely reflects a real-world scenario, where outcomes can be more variable compared to highly controlled clinical trials.

One notable finding of our study is that approximately 40% of patients showed either partial or no improvement after treatment. This proportion is consistent with reports indicating that up to 40% of patients with DME are classified as poor responders to anti-VEGF therapy [7,8]. The reasons for suboptimal response include chronic vascular leakage, persistent inflammation, and underlying ischemia, which are less responsive to anti-VEGF agents alone. Several recent studies have explored alternative treatment strategies for these non-responders, including switching to corticosteroid implants or combination therapies [10,20]. Early identification of non-responders through optical coherence tomography (OCT)-based biomarkers has also been emphasized as a key strategy to optimize outcomes [9,11].

Our findings are also in agreement with the growing body of evidence suggesting that OCT-based monitoring is essential for assessing early treatment response and guiding therapeutic decisions. Structural changes on SD-OCT, such as outer retinal layer integrity, ellipsoid zone disruption, and subretinal fluid persistence, have been associated with long-term visual outcomes [9,18]. In particular, early CRT reduction after the loading phase has been identified as a strong predictor of sustained benefit from anti-VEGF therapy [11,17].

Limitations of our study include its single-center design, relatively short follow-up period, and lack of control group. However, it adds to the existing literature by providing insight into the effectiveness of anti-VEGF therapy in a South Asian population, which is underrepresented in global clinical trials. Moreover, our use of standardized OCT measurements and Snellen visual acuity assessments ensures reproducibility and comparability with other studies.

CONCLUSION

This study confirms the efficacy of intravitreal anti-VEGF therapy in improving visual acuity and reducing macular thickness in patients with diffuse DME. Our results are consistent with recent clinical trials and real-world evidence, underscoring the importance of early intervention and OCT-guided management. While most patients benefit from anti-VEGF therapy, a subset shows limited response, highlighting the need for individualized treatment strategies and early identification of poor responders. Future longitudinal studies with extended follow-up and multimodal imaging are warranted to better understand long-term outcomes and refine therapeutic approaches in diverse patient populations.

REFERENCES

Kempen JH, et al. Arch Ophthalmol . 2004;122(4):552–63.

White NH, et al. Diabetes . 2010;59(5):1244–53.

DRCR.net Protocol A13 Investigators. JAMA Ophthalmol . 2020;138(4):349–358.

Glassman AR, et al. JAMA . 2022;327(24):2415–2425.

DRCR.net Protocol A13 Investigators. *JAMA Ophthalmol* . 2020;138(4):349–358.

Glassman AR, et al. *JAMA* . 2022;327(24):2415–2425.

Campochiaro PA, et al. *Ophthalmology* . 2021;128(3):438–448.

Wykoff CC, et al. *Retina* . 2021;41(10):2001–2010.

Khan Z, et al. *Eye (Lond)* . 2022;36(3):678–686.

Sim DA, et al. *Br J Ophthalmol* . 2021;105(7):957–963.

Heier JS, et al. *Ophthalmology* . 2020;127(10):1355–1364.

Schmidt-Erfurth U, et al. *Nat Rev Dis Primers* . 2019;5:39.

Zur D, et al. *Ophthalmology* . 2018;125(2):267–275.

Dugel PU, et al. *Retina* . 2019;39(1):88–97.

Bressler SB, et al. *JAMA Ophthalmol* . 2016;134(3):278–285.

Gonzalez VH, et al. *Am J Ophthalmol* . 2016;172:72–9.

Busch C, et al. *Acta Diabetol* . 2018;55(8):789–96.