

Comparison of Anti-VEGF Therapy and Corticosteroids in the Management of Uveitic Macular Edema

Sandeep Kumar, Fariha Sher Wali, Adnan Abdul Majeed, Sanam Munawar Ul Islam, Hifsa Pirzado, Reena

ABSTRACT

Objective: To compare the anti-VEGF therapy and corticosteroids in improving best-corrected visual acuity (BCVA) and reducing central macular thickness (CMT) in UME patients.

Study design and Setting: A Prospective Cohort Study conducted at Sindh Institute of Ophthalmology and Vision Sciences, Hyderabad

Methodology: In this study 120 patients with UME were enrolled and 60 patients who received anti-VEGF Bevacizumab were placed Group A and those who were given Corticosteroids: intravitreal triamcinolone acetonide were placed in Group B. Primary outcomes were BCVA (logMAR), CMT and visual acuity improvement at 6 months. The secondary outcome was the total number of intravitreal injections administered per patient over 6 months, along with treatment-related adverse events.

Results: Both groups showed significant within-group improvement in BCVA and CMT, with a significant Group $\times$ Time interaction for BCVA and CMT ($p < 0.001$). The corticosteroid group had significantly greater CMT reduction at 1 month and all subsequent measurements (between group $p < 0.001$) and greater improvement in the number of lines of visual acuity at 6 months (between group $p = 0.019$); however, the between-group difference in continuous BCVA at 6 months was not significant ($p = 0.099$). IOP elevation ($p = 0.002$) and cataract progression ($p = 0.001$) were significantly more common with corticosteroids.

Conclusion: Intravitreal corticosteroid therapy was associated with greater anatomical improvement and a higher proportion of patients achieving clinically meaningful visual acuity gain compared with anti-VEGF therapy in uveitic macular edema, though this benefit came with a significantly higher risk of IOP elevation and cataract progression.

Keywords: Anti-VEGF, Bevacizumab, Central Macular Thickness, Corticosteroids, Uveitic macular edema

How to cite this Article:

Kumar S, Wali FS, Majeed AA, Islam SMU, Pirzado H, Reena. Comparison of Anti-VEGF Therapy and Corticosteroids in the Management of Uveitic Macular Edema, J Bahria Uni Med Dental Coll. 2026;16(4):1014-22 DOI: <https://doi.org/10.51985/JBUMDC20261091>

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non Commercial License (<http://creativecommons.org/licenses/by-nc/4.0>) which permits unrestricted non commercial use, distribution and reproduction in any medium, provided the original work is properly cited.

Sandeep Kumar

Senior Registrar, Department of Ophthalmology
Sindh Institute of Ophthalmology and Vision Sciences, (SIOVS)
Hyderabad
Email: drsandeepbansari@gmail.com

Fariha Sher Wali

Associate Professor, Department of Ophthalmology
SIOVS, Hyderabad
Email: fariha80@gmail.com

Adnan Abdul Majeed

Senior Registrar, Department of Ophthalmology
SIOVS, Hyderabad
Email: adnan.majeed@siovs.edu.pk

Sanam Munawar Ul Islam

Senior Registrar, Department of Ophthalmology
SIOVS, Hyderabad
Email: drsanam.munawar@gmail.com

Hifsa Pirzado

Medical Officer, Department of Ophthalmology
SIOVS, Hyderabad
Email: hafsapirzado@gmail.com

Reena

Senior Registrar, Department of Ophthalmology
SIOVS, Hyderabad
Email: reena@siovs.edu.pk

Received: 01-07-2026

Accepted: 28-09-2026

1st Revision: 21-07-2026

2nd Revision: 28-8-2026

INTRODUCTION

Uveitis is an umbrella term for a group of intraocular inflammatory conditions, one of the most important preventable causes of blindness in the world. The most important structural problem related to it is uveitic macular edema (UME) that occurs in approximately 30-40% of chronic uveitis cases and contributes up to 35% of the visual loss in uveitis. It was noted that UME is the key factor which affects the long-term visual outcome in all subsets of uveitis and the treatment of UME is a long-term problem as it is multifactorial in its aetiology and has varying treatment responses. The natural history and treatment paradigms of UME that are applicable to non-inflammatory macular disease can be affected by UME.^{1,2} The intraocular inflammation in the pathogenesis of UME results in the disruption of the blood-retinal barrier, secondary to pro-inflammatory cytokines and vascular endothelial growth factor (VEGF) that affect the permeability of the vascular wall and induce accumulation of fluid in the macula. There is a correlation between VEGF upregulation in uveitic vitreous, supporting the use of anti-VEGF therapy for UME.³ Bevacizumab and corticosteroids work in different but

complementary ways, the corticosteroid therapy works at the top level of the cytokine cascade that leads to oedema and VEGF production while anti-VEGF therapy acts further downstream by blocking the VEGFR and vimentin that control vascular permeability.⁴

Corticosteroids have been the mainstay of the management of UME. The POINT trial compared three regional corticosteroid strategies for UME — periocular triamcinolone, intravitreal triamcinolone, and the intravitreal dexamethasone implant — and found that both intravitreal routes produced significantly greater CMT reduction and BCVA improvement than the periocular route, with the dexamethasone implant showing noninferiority to intravitreal triamcinolone rather than superiority. However, despite the proven effectiveness of anti-VEGF agents in other forms of macular edema, their favourable intraocular pressure and cataractogenic profile has made them attractive for patients with corticosteroid related co-morbidities.⁵ The MERIT trial showed that dexamethasone implant was more effective at 12 weeks at reducing CMT by 35% compared to ranibizumab by 22%, with ranibizumab not producing a statistically significant improvement in BCVA at any timepoint, suggesting the superiority of corticosteroid agents in terms of short-term outcome.⁶ Different studies conducted in patients with macular edema also support this trend, but cannot be directly applied to the uveitic situation.⁷⁻⁹ However, it is difficult to extrapolate the results from retinal vein occlusion (RVO) to UME, as there is no active inflammatory process in these conditions as existed in diabetic macular edema (DME) during the short-term CMT reduction, which was larger with intravitreal steroids than anti-VEGF.^{10,11} With this evidence, there is still a need for more investigation as there has been no prospective study comparing anti-VEGF and corticosteroid use specifically for UME that has followed for an extended period of time. In the context of vision loss due to uveitis, UME is a constantly underrepresented group of diseases, especially in the context of macular edema studies. In South Asian population, infectious diseases being the leading cause, such as TB associated uveitis, and treatment response to the uveitis may vary from that of most clinical trials of inflammatory uveitis in the Western world.¹² Therefore, a cohort study was designed to compare the use of intravitreal anti-VEGF therapy and intravitreal corticosteroid use in UME in SIOVS Hyderabad Pakistan. The main goal of this study was to compare BCVA, improvement in visual acuity at 6 month and mean CMT in the two treatment groups. Secondary outcome was the total number of intravitreal injections/patient over 6 months' duration and treatment related adverse events (increase in intraocular pressure, cataract progression, endophthalmitis) as well as loss to follow-up.

METHODOLOGY

The study was a prospective cohort design in which Patients were recruited over a 12-month period (March 2025–March

2026); each enrolled patient was followed for 6 months from their baseline visit, at Sindh Institute of Ophthalmology & Visual Sciences (SIOVS), Hyderabad, Sindh, Pakistan. Approval form Ethical Review committee of SIOVS approval was obtained vide letter number SIOVS/EXEC.DIR/09/03/2025. Uveitic Macular Edema patients, diagnosed in Retina and Uvea clinics were divided into two groups: Group A (anti-VEGF bevacizumab 1.25 mg/0.05 mL) and Group B (anti-corticosteroid triamcinolone acetonide 4 mg/0.1 mL). Treatment allocation was based on the clinical diagnosis and routine practice of the ophthalmologist.

Patients included were those aged = 18 years, had CMT = 300 μ m and a best corrected visual acuity (BCVA) between 6/12 and 6/120 (logMAR 0.3–1.3) of the study eye, and a confirmed diagnosis of uveitis regardless of anatomical subtype (anterior, intermediate, posterior or panuveitis). Patients were ineligible if macular edema was not caused by uveitis, had occurred in the past 3 months due to intravitreal injection, had significant media opacity that prevented good imaging, had an active ocular infection, uncontrolled glaucoma (IOP > 21 mmHg on = 2 medications), history of corticosteroid-induced IOP elevation, pregnancy, or had a systemic contraindication to anti-VEGF (recent thromboembolic event in the last 3 months) or failure to follow-up schedule. OpenEpi Version 3.01 was used for the sample size calculations using 72% for the presumed proportion for the corticosteroid group (which represents a 20-percentage-point improvement compared with baseline) and =2 Snellen lines for improvement at 6 months for the baseline, based on a directional BCVA superiority of dexamethasone implant over ranibizumab from the MERIT trial.⁶ A study comparing the two treatments in UME has not reported exact head-to-head proportions at 6 months; therefore, this was used as a planning assumption. A sample size of 55 patients per group was estimated to achieve a power of 80% and an α level of 0.05; a 10% attrition allowance was targeted to obtain 60 patients per group ($n = 120$). All patients had a comprehensive baseline assessment at enrolment (Visit 0) with clinical history (age, sex, duration of uveitis symptoms, previous treatment, systemic comorbidities), BCVA on standardised Snellen chart at 6 metres translated to logMAR, anterior chamber cells and flare assessed with slit-lamp biomicroscopy, CMT recorded as mean retinal thickness within the central 1 mm ETDRS subfield. Clinically indicated fundus fluorescein angiography performed. Directed systemic investigations included chest radiography, IGRA or Mantoux test, serum ACE, ANA, ANCA, HLA-B27 and syphilis serology.

Group A patients were given an initial anti-VEGF injection at baseline, followed at the monthly visits with additional anti-VEGF injections as needed (pro re nata [PRN]). All patients in Group B received one corticosteroid injection at baseline; patients were allowed to be retreated at or after = 12 weeks if persistent or recurrent macular edema was found

on SD-OCT, and all were given concomitant systemic therapy as indicated by the treating specialist. BCVA, IOP and CMT were used for the follow-up visits at month 1, 3 and 6. Adverse events such as IOP elevation (more than 21 mmHg or more than 10 mmHg from baseline), cataract progression, endophthalmitis and loss to follow up were systematically documented. The primary outcomes included: (i) BCVA (logMAR) at each follow-up visit; (ii) improvement in visual acuity at 6 months (defined as improvement of ≥ 2 Snellen lines ($= 0.2$ logMAR) from baseline); and (iii) mean CMT (μm) on SD-OCT. All participants provided written informed consent before they were enrolled. IBM SPSS Statistics Version 24.0 (IBM Corp., Armonk, NY, USA) was used to conduct all statistical analyses. Shapiro Wilk test was used to assess the normality of quantitative data and presented as mean $\pm$ SD or median (IQR) as appropriate. Categorical variables were summarized in terms of frequencies and percentages. Independent samples t-test and Mann-Whitney U test were used for continuous data and Pearson's chi-square and Fisher's exact test for categorical data were used for between group comparisons. A mixed model for repeated measures (MMRM) with an unstructured covariance structure, fitted by restricted maximum likelihood (REML) was used to test for changes in BCVA, CMT, and IOP across time, while accounting for within-subject correlation and missing data under the assumption of missing at random. Intragroup differences from baseline were evaluated with Bonferroni adjusted contrasts within the MMRM framework. Independent predictors at 6 months of ≥ 2 -line improvement were identified using a binary logistic regression model, results of which are presented as adjusted odds ratios (aOR) and 95% confidence intervals (CI). The secondary outcome was the number of intravitreal injections per patient received during the 6-month period, as well as the incidence of adverse events associated with treatment (IOP elevation, progression of cataract, endophthalmitis) and loss of follow-up. A p-value of < 0.05 was deemed to be statistically significant.

RESULTS

A total of 120 patients with uveitic macular edema were enrolled, 60 of which were placed in the anti-VEGF group and 60 to the corticosteroid group. The overall cohort comprised 57 males (47.5%) and 63 females (52.5%), with a mean age of 40.74 ± 11.91 years (range 18–67 years). At the time of enrolment, the mean duration of uveitis was 15.04 ± 15.37 months (range 3–84 months); and the chronicity of uveitis was very variable between participants. With respect to uveitis anatomical subtype, anterior uveitis was the most common type, with 36 patients (30.0%), followed by panuveitis (25.8%), intermediate uveitis (24.2%) and posterior uveitis (20.0%). In terms of aetiology, the most common cause was tuberculosis associated uveitis (30.8%) followed by idiopathic uveitis (29.2%), other (15.0%), HLA-B27 associated (14.2%) and sarcoidosis (10.8%).

Fifty-seven patients (47.5%) did not have systemic

comorbidities. The most common co-morbidity was hypertension 32 (26.7%), followed by diabetes mellitus 27 (22.5%) and other systemic conditions 04 (3.3%). Of those enrolled 43 (35.8%) received a previous intravitreal injection and 77 (64.2%) did not receive any intravitreal injection. (Table 1)

Table 2 shows the MMRM analyses of all the 3 primary outcome variables. Among the three variable the Group effect reached statistical significance level for CMT only ($p=0.001$), showing difference in CMT between groups in the entire follow up. A statistically significant Time effect was observed for BCVA, CMT and IOP ($p=0.001$) at all 4 different measurement time. In each of the three main outcome measures, the interaction between Group $\times$ Time was significant (all $p<0.001$), indicating that the trajectories of the two groups differed significantly throughout the entire follow-up period. The estimated marginal mean is graphically represented in table 3. The patients in corticosteroid group consistently shows more reduction in BCVA (logMAR) as compared to Anti-VEGF group at all 4 points. No difference was observed between groups ($p > 0.05$) however, within group difference was statistically significant ($p < 0.05$). The corticosteroid group had greater reductions in macular thickness at all post-baseline time points than the anti-VEGF group, the difference in which was significant from 1 month and became more marked with increasing time. The reduction in CMT from baseline was highly significant in both groups ($p < 0.001$), confirming a genuine anatomical treatment response with both therapies. Baseline IOP was slightly but significantly lower in the corticosteroid group (13.82 vs 14.76 mmHg, $p=0.032$), a difference addressed in the Limitations. At 1 month, there was a notable between-group difference, with transient increase in IOP in the corticosteroid group that subsequently falls back towards baseline levels at 3 and 6 months. Within-group IOP change from baseline was significant in both groups ($p < 0.001$), highlighting the different temporal IOP changes of these two treatment modalities during the follow-up period.

In Table 4, the proportion of patients who had a clinically meaningful improvement in VA and the rates of adverse events and treatment burden are shown. The corticosteroid group had a significantly higher rate of clinically meaningful (≥ 2 -line) visual acuity improvement at 6 months (78.3% vs 58.3%, $p = 0.019$) than the anti-VEGF group, consistent with the trajectory seen in the MMRM analysis. As for ocular safety, the corticosteroid group had significantly more IOP elevation and cataract progression than the anti-VEGF group ($p=0.002$ and $p=0.001$ respectively). There was no progression of cataract in the anti-VEGF group, while progression occurred in a significant number of patients in the corticosteroid arm. There were no between group difference for endophthalmitis ($p = 0.496$) and it was rare in both groups. The two groups had similar and low rates of loss to follow up ($p = 1.000$), suggesting equal loss to

follow up which is not likely to have created differential bias. In terms of treatment burden, the number of intravitreal injections administered over 6 months was significantly higher for the anti-VEGF group than for the corticosteroid group ($p < 0.001$), which is due to the PRN re-treatment regimen of anti-VEGF treatments compared with the drug-release time of intravitreal corticosteroid injections. This variation in injection frequency has implications for aspects of patient adherence, utilization of health care resources and the practicability of treatment in resource-constrained

environments. The choice of corticosteroid, compared with anti-VEGF, was the only independent factor associated with the outcome, with an odds ratio of ~ 2.6 . (Table 5). In this model, none of the patient characteristics (age, sex, log VAS, retinal thickness, prior treatment experience, etiology, comorbidities, or uveitis type) was a significant predictor of the outcome.

DISCUSSION

In this prospective cohort study, the efficacy and safety of intravitreal anti-VEGF therapy and intravitreal corticosteroids

Table 1: Demographics & Baseline characteristics (n=120)

Characteristic	Anti-VEGF (n=60)	Corticosteroid (n=60)	p-value
Age, years, mean±SD	40.15±13.27	41.33±10.44	0.588†
Uveitis duration, months, mean±SD	14.87±11.04	15.22±18.82	0.901†
Gender, n (%)			
Male	31 (51.7)	26 (43.3)	0.361‡
Female	29 (48.3)	34 (56.7)	
Aetiology, n (%)			
TB-associated	15 (25.0)	22 (36.7)	0.404‡
Sarcoidosis	7 (11.7)	6 (10.0)	
HLA-B27 associated	11 (18.3)	6 (10.0)	
Idiopathic	16 (26.7)	19 (31.7)	
Other	11 (18.3)	7 (11.7)	
Anatomical subtype, n (%)			
Anterior	22 (36.7)	14 (23.3)	0.342‡
Intermediate	12 (20.0)	17 (28.3)	
Panuveitis	16 (26.7)	15 (25.0)	
Posterior	10 (16.7)	14 (23.3)	
Comorbidities, n (%)			
Diabetes	12 (20.0)	15 (25.0)	0.921*
Hypertension	16 (26.7)	16 (26.7)	
None	30 (50.0)	27 (45.0)	
Other	2 (3.3)	2 (3.3)	
Prior intravitreal injections, n (%)			
No	38 (63.3)	39 (65.0)	0.849‡
Yes	22 (36.7)	21 (35.0)	
Baseline BCVA, logMAR, mean±SD	0.80±0.21	0.79±0.21	0.794†
Baseline CMT, µm, mean±SD	426.9±80.3	419.0±64.3	0.552†
Baseline IOP, mmHg, mean±SD	14.76±2.18	13.82±2.56	0.032†§

† t test applied, ‡ Chi square test applied, * Fisher exact test applied, § significant p value

Table 2: Mixed-Effects Model for Repeated Measures (MMRM) Type III Tests of Fixed Effects

Outcome Variable	Group Effect	Time Effect	Group $\times$ Time Interaction
BCVA (logMAR)	F(1,118)=1.710 p=0.194	F(3,118)=833.197 p<0.001	F(3,118)=20.614 p<0.001
CMT (μ m)	F(1,118)=11.416 p=0.001	F(3,118)=690.354 p<0.001	F(3,118)=29.558 p<0.001
IOP (mmHg)	F(1,118)=1.855 p=0.176	F(3,118)=58.934 p<0.001	F(3,118)=41.741 p<0.001

Group effect: overall between-group difference pooled across timepoints, Time effect: change over time pooled across groups. Group $\times$ Time interaction: differential trajectory between groups over time

Table 3: Estimated Marginal Means (SE) with 95% Confidence Intervals by Group and Time point BCVA, CMT, and IOP

Outcome	Timepoint	Anti-VEGF (n=60) Mean (SE) [95% CI]	Corticosteroid (n=60) Mean (SE) [95% CI]	Between-group p†
		Log MAR	Log MAR	
BCVA (log MAR) Group ×Time p<0.001	Baseline	0.802 (0.027) [0.748, 0.855]	0.792 (0.027) [0.738, 0.845]	0.788
	1 Month	0.723 (0.028) [0.668, 0.779]	0.660 (0.028) [0.604, 0.715]	0.095
	3 Months	0.631 (0.029) [0.574, 0.688]	0.567 (0.029) [0.510, 0.624]	0.052
	6 Months	0.592 (0.031) [0.532, 0.653]	0.526 (0.031) [0.465, 0.586]	0.099
	Within-group p-value‡	Anti-VEGF: <0.001	Corticosteroid: <0.001	—
CMT (µm) Group ×Time p<0.001	Baseline	426.9 (9.4) [408.3, 445.5]	419.0 (9.4) [400.4, 437.6]	0.548
	1 Month	373.5 (8.4) [356.8, 390.2]	340.8 (8.4) [324.1, 357.5]	0.012
	3 Months	352.0 (7.8) [336.4, 367.5]	299.7 (7.8) [284.1, 315.2]	<0.001
	6 Months	325.9 (8.1) [309.8, 342.0]	267.2 (8.1) [251.1, 283.3]	<0.001
	Within-group p-value‡	p <0.001	p <0.001	—
IOP (mmHg) Group ×Time p<0.001	Baseline	14.76 (0.31) [14.16, 15.37]	13.82 (0.31) [13.21, 14.43]	0.033
	1 Month	14.96 (0.36) [14.24, 15.67]	16.93 (0.36) [16.21, 17.65]	<0.001
	3 Months	15.12 (0.39) [14.34, 15.90]	15.95 (0.39) [15.17, 16.73]	0.038
	6 Months	14.87 (0.37) [14.14, 15.61]	15.44 (0.37) [14.70, 16.17]	0.211
	Within-group p-value‡	p <0.001	p <0.001	—

Values are estimated marginal mean (standard error) [95% confidence interval]. †Between-group p-values (Bonferroni-adjusted) at each timepoint. ‡Within-group p-values represent Bonferroni-adjusted change from baseline over 6 months. BCVA: best-corrected visual acuity; CMT: central macular thickness; IOP: intraocular pressure; SE: standard error; CI: confidence interval. Bold p-values indicate statistical significance (p = 0.05)

Table 4: Comparison of Visual Acuity Improvement and Adverse Events Between Anti-VEGF and Corticosteroid Groups

Predictor	aOR	95% CI	p-value
Corticosteroid vs. Anti-VEGF (Ref)	2.59	1.12–5.98	0.026
Age (per year)	1.01	0.98–1.05	0.563
Baseline BCVA (log MAR)	0.21	0.03–1.60	0.133
Baseline CMT (per µm)	1.00	0.995–1.006	0.919
Sex: Male/Female (Ref)	1.58	0.69–3.58	0.278
Prior intravitreal injection (Ref: Naïve)	1.08	0.45–2.58	0.866
Aetiology: infectious vs. non-infectious (Ref)	0.60	0.26–1.38	0.227
Comorbidity: any vs. none (Ref)	0.99	0.42–2.35	0.981
Uveitis type: non-anterior vs. anterior (Ref)	1.04	0.43–2.54	0.929

Table 5: Predictors of ≥2-line visual acuity improvement at 6 months

Outcome / Adverse Event	Anti-VEGF (n=60) n (%)	Corticosteroid (n=60) n (%)	Total (n=120) n (%)	p-value
VA Improvement = 2 Snellen lines at 6 months, n (%)	35 (58.3%)	47 (78.3%)	82 (68.3%)	0.019
IOP Elevation, n (%)	1 (1.7%)	11 (18.3%)	12 (10.0%)	0.002
Cataract Progression, n (%)	0 (0.0%)	11 (18.3%)	11 (9.2%)	0.001
Endophthalmitis, n (%)	0 (0.0%)	2 (3.3%)	2 (1.7%)	0.496
Lost to Follow-up, n (%)	5 (8.3%)	4 (6.7%)	9 (7.5%)	1.000
Total Injections (Mean ±SD)	5.30 (2.036)	2.08 (1.154)	3.69 (2.307)	<0.001

Chi-square test used for VA improvement; Fisher's exact test used for all adverse event comparisons. Bold p-values indicate statistical significance (p = 0.05). VA: visual acuity; IOP: intraocular pressure

OR: odds ratio; aOR: adjusted odds ratio; CI: confidence interval.

were compared for the treatment of uveitic macular edema for a follow-up period of 6 months in a tertiary ophthalmic centre in Hyderabad, Pakistan. The main finding was that corticosteroid therapy was associated with better anatomical results (greater central macular thickness reduction) and a significantly higher proportion of patients achieving clinically meaningful (≥ 2 -line) improvement in VA at 6 months compared to anti-VEGF therapy. The mixed-effects model for repeated measures showed a significant Group $\times$ Time interaction for all three primary outcome variables BCVA, CMT and IOP, indicating that the two treatment modalities had very different clinical courses during the observation period. This, to our knowledge, is one of the limited prospective, comparative studies on these two treatment modalities specifically in uveitic macular edema in South Asian context where tuberculosis-associated uveitis is the predominant aetiological type.

In both treatment groups, BCVA at 6 months was significantly higher than at baseline ($p < 0.001$) as would be expected with treatment of UME, regardless of the therapy used. In the context of the large cohorts mentioned above, uveitic eyes with macular edema had a 6-month rate of ≥ 2 lines visual acuity improvement of 68.3%; a figure that favourably outperformed the 45% improvement rate reported by Levin et al.¹³ The corticosteroid group had a rate of ≥ 2 -line improvement of 78.3% versus 58.3% for the anti-VEGF group ($p = 0.019$). The finding is consistent with the study by POINT which concluded that intravitreal dexamethasone implant is the most effective method of corticosteroid delivery in UME compared to ranibizumab,⁵ and another study found that intravitreal dexamethasone implant yielded statistically significant gains in BCVA at all timepoints, while intravitreal ranibizumab did not produce any statistically significant BCVA gain at any timepoint.⁶ Notably, the intravitreal triamcinolone arm of POINT, the same agent used in our corticosteroid group achieved BCVA gains statistically indistinguishable from the dexamethasone implant, supporting the applicability of dexamethasone-implant-based comparative evidence to our triamcinolone findings. The within-group improvement in BCVA seen in our anti-VEGF group (as compared to the lack of any such improvement in the MERIT trial) may be attributable to the longer duration of our study (6 months as opposed to 12 weeks in MERIT) and to differences in the anti-VEGF agent used, our study used bevacizumab exclusively, whereas MERIT evaluated ranibizumab. Even if corticosteroids have shown greater short term functional benefit in inflammatory diseases, anti-VEGF therapy may provide meaningful visual results over 24 months, supporting anti-VEGF as a treatment option in the uveitic setting as long as it is given for long enough periods of time.¹⁴

The most consistent and clinically most compelling finding of this study was the anatomical superiority of corticosteroid therapy, reflected in greater CMT reduction. The

corticosteroid group showed a mean reduction in CMT of 151.8 μm from baseline to 6 months, while the anti-VEGF group showed a mean reduction of 101.0 μm from baseline to 6 months, which represents about 50 μm more reduction that was statistically significant beginning at 1 month. This is mechanistically understandable: steroids have been shown to inhibit the whole upstream cytokine cascades, such as TNF- α , IL-6 and VEGF, which all contribute to the blood-retinal barrier failure in uveitic macular edema, while anti-VEGF agents specifically target the downstream VEGF-mediated permeability mechanism and don't block the first line of the inflammatory cascade. The upregulation of VEGF in uveitic eyes is merely secondary and dependent upon the underlying inflammatory process, which means that drugs that are simply targeted against VEGF are likely to have less efficacy in a condition in which inflammation is the primary cause.³ An experimental uveitis model showed that bevacizumab and corticosteroid act through complementary but non-overlapping pathways.⁴ There have been several meta-analyses of diabetic macular edema studies, and all of them have shown greater CMT reductions with intravitreal steroids than with anti-VEGF alone. Studies showed that corticosteroid is superior for short-term CMT reduction in DME,^{7,8} and our findings were consistent with this pattern in the uveitic macular edema population as well; a review in 2024 reinforced corticosteroids' anatomical benefit over anti-VEGFs in DME.¹⁵ A similar finding was shown by Koc et al., who showed that dexamethasone implants were superior to anti-VEGF treatment, especially in treatment-resistant DME.¹⁶ Our CMT change in the corticosteroid group is consistent with the 35% CMT change reported in the MERIT trial for dexamethasone implant, indicating that for CMT, the anatomic changes induced by corticosteroid treatment are generalizable to all macular edema subtypes.⁶

Among the safety profile, there was a higher rate of IOP elevation (18.3% in the CST group vs 1.7% in the anti-VEGF group, $p = 0.002$) and progression of cataract (0% in the anti-VEGF group vs 18.3% in the CST group, p value 0.001) in the CST group. These rates are within the range of the adverse effect profile on the eye that has been seen in the landmark corticosteroid intravitreal trials. In the dexamethasone implant arm of the POINT trial there were 25% more cases of elevated IOP, and the MERIT trial found that the corticosteroid arm had higher rates of elevated IOP and lens opacity than the ranibizumab arm.^{5,6} A study specifically analyzing DME patients with coexisting cataract found that dexamethasone implant was associated with significantly greater cataract progression than anti-VEGF therapy,¹⁷ consistent with our findings in the uveitic population. The transient but dramatic IOP increase noted at 1 month (mean 16.93 mmHg in the corticosteroid group, 14.96 mmHg in the anti-VEGF group, $p < 0.001$) is a typical early steroid response that can be controlled with topical IOP-lowering medications, but should be carefully monitored

in patients with pre-existing glaucoma or ocular hypertension. A similar endophthalmitis rate was reported in the dexamethasone implant group compared to anti-VEGF intravitreal injection group which is concordant with our results ($p = 0.496$).¹⁸ These different safety profiles between the two drugs reinforce the necessity to make decisions on the use of a corticosteroid vs anti-VEGF drug in UME treatment based on patient-specific risk assessment, which should take into account lens status, baseline IOP, and glaucoma history.

The absolute number of injections given during the study period was a secondary but clinically important parameter that was different between the two treatment approaches. Anti-VEGF treatments are typically given more often than long-acting corticosteroid drugs such as dexamethasone implant, which provides a sustained drug release for 4-6 months. Corticosteroids have also been shown to be injection-sparing in persistent diabetic macular edema (DME) when used in combination with bevacizumab.¹⁹ A similar study found that anti-VEGF and steroid combination therapy in DME decreased the total number of injections without compromising functional outcomes.²⁰ The injection burden consideration has even greater clinical and socioeconomic importance in SIOVS because of the direct influence on patient compliance and accessibility in resource-limited environments in which the cost and frequency of intravitreal injections can have a significant impact on patients. A recent (2024) study of combination anti-VEGF and dexamethasone implant therapy for RVO-related macular edema found that combination therapies are effective for optimising anatomical outcomes and maintaining injection frequency,²¹ while another 2024 study, showed that alternate corticosteroid and anti-VEGF therapy was feasible in RVO-related macular edema and may be especially beneficial in UME patients who are partially responsive to anti-VEGF therapy alone.²² The mechanism of action of these two drug classes is also likely to be complementary, and the meta-analysis showed that the combination of anti-VEGF and intravitreal corticosteroid therapy in neovascular AMD resulted in better anatomical outcomes than anti-VEGF alone, bolstering the rationale for combination or sequence therapy in the uveitic UME context, which remains to be prospectively evaluated.²³ Switching non-responsive anti-VEGF eyes to corticosteroid therapy has similarly been shown to improve outcomes in other neovascular conditions, supporting the case for exploring this sequencing strategy in UME as well.²⁴

Another unique characteristic of this group was that the majority had tuberculous uveitis (30.8%) with similar prevalence in Pakistan and in South Asia as a whole. The aetiological profile of our cohort is markedly different from that of most other UME trials, which were mostly conducted in the West, such as the MERIT and POINT trials. It was highlighted that therapeutic recommendations in UME are based on studies in predominantly non-infectious populations,

making it hard to extrapolate these to TB-endemic populations. In this mainly TB-endemic group, we believe that the use of corticosteroids was effective and safe when given with appropriate systemic anti-tubercular therapy with no documented cases of TB reactivation due to corticosteroid use.^{1,2} A recent 2024 systematic review by Kumar et al.,²⁵ and Cheng and Liu¹⁵ underscored an evidence gap that this study addresses as they both found the evidence base for comparative anti-VEGF versus corticosteroid treatment mostly came from non-inflammatory macular disease, providing a region-specific and clinically actionable evidence base for ophthalmologists in high-TB-burden areas.

The aetiological composition of our cohort — with TB-associated uveitis as the leading cause (30.8% overall), followed by idiopathic and HLA-B27-associated disease — reflects the burden of infectious and autoimmune uveitis reported in this region.²⁶ Notably, outcomes in TB-associated UME may differ from other aetiologies given the concurrent need for antitubercular therapy and differing inflammatory kinetics, an area highlighted by recent characterization of UME specifically within ocular tuberculosis populations.²⁷ Future subgroup analyses stratified by aetiology may help clarify whether treatment response to anti-VEGF versus corticosteroid therapy varies by underlying cause. Some limitations should be recognized in the present study. First, this was a non-randomised prospective cohort with treatment allocation based on the attending clinician any patients pre-existing glaucoma or sensitivity to corticosteroid would have been more likely to be allocated to the anti-VEGF group, which may have slightly underestimated the true safety disadvantage of corticosteroid use in an unselected population. Similarly, allocation may have been influenced by baseline disease severity or anatomical subtype for instance, clinicians may have preferentially selected corticosteroid therapy for eyes with more treatment-resistant or severe edema, or conversely reserved it for less complex cases where a stronger anti-inflammatory response was anticipated. Either pattern would confound the observed between-group differences in CMT and visual acuity, and the reported associations should therefore be interpreted as hypothesis-generating rather than evidence of causal treatment superiority. Secondly, the study was carried out at a single tertiary centre, which also ensured a standardised clinical assessment and imaging protocol but may restrict the generalisability of the results to other healthcare settings. Third, the results from the 6-month follow-up period may not accurately represent long-term disease outcomes, or the likelihood of recurrence after stopping treatment or cumulative adverse effect burden from repeated corticosteroid use. Fourth, much of the comparative RCT evidence discussed (MERIT) evaluated the dexamethasone implant rather than triamcinolone acetonide, which differ in pharmacokinetics — a sustained-release device versus a crystalline suspension with a more transient peak-and-trough profile. While the

POINT trial's intravitreal triamcinolone arm showed anatomical and visual outcomes comparable to the implant, supporting the relevance of implant-based comparisons for efficacy, the two agents' differing release kinetics likely account for the early, transient IOP spike we observed at 1 month, which may not generalize to sustained-release formulations. Fifth, a differential between groups was assumed based on the results from the MERIT trial, and no published study has reported directly on 6-month visual improvement proportions in UME and this is a methodological caveat. Last, there are no standardized severity grading of uveitis at each follow-up visit, which makes it difficult to completely control for disease activity as a time-varying confounder.

CONCLUSION

This study showed that intravitreal corticosteroid therapy was associated with greater anatomical improvement (CMT reduction) and a higher proportion of patients achieving clinically meaningful visual acuity gain compared with anti-VEGF therapy in uveitic macular edema over 6 months; however, the two treatments did not differ significantly in continuous BCVA change. These anatomical and visual acuity benefit came at the price of significantly increased incidence of IOP elevation and cataract development, and this highlights the need to tailor treatment selection for each patient, depending on their ocular risk profile, lens status, glaucoma history, and the underlying cause of the disease in UME. Anti-VEGF therapy is clinically viable and safer, especially in phakic patients, patients with high baseline intraocular pressure, or patients where it is not possible to monitor for the effects of corticosteroid therapy. Future studies should include multicentre RCTs with longer follow-up periods, with uveitis activity grading standardised at every centre and with aetiological subgroups, with infectious and non-infectious uveitis as specific subgroups, to confirm optimal treatment algorithms for uveitic macular edema in different clinical settings.

Conflict of Interest: None

Fundings: No funding source

Use of Artificial Intelligence (AI) Disclosure: There is no AI tool used.

Authors Contribution:

Sandeep Kumar: Conceptualization & Design
Fariha Sher Wali: Methodology
Adnan Abdul Majeed: Drafting the manuscript
Sanam Munawar Ul Islam: Data analysis
Hifsa Pirzado: Interpretation of data
Reena: Provided supervision & Final review

REFERENCES

- Koronis S, Stavarakas P, Balidis M, Kozeis N, Tranos PG. Update in treatment of uveitic macular edema. *Drug Des Devel Ther.* 2019 Feb 19;13:667-680. doi: 10.2147/DDDT.S166092.
- Tallouzi MO, Moore DJ, Barry RJ, Calvert M, Mathers J, Murray PI, et al. The effectiveness of pharmacological agents for the treatment of uveitic macular edema (UMO): a systematic review. *Ocul Immunol Inflamm.* 2019;27(4):658–80. doi: 10.1080/09273948.2019.1569243.
- Teper SJ. Update on the Management of Uveitic Macular Edema. *J Clin Med.* 2021 Sep 14;10(18):4133. doi: 10.3390/jcm10184133.
- Ayyıldız O, Durukan AH, Ozgurtas T, Gunal A. A comparison of intravitreal bevacizumab and steroid activity in an experimental uveitis model. *Curr Eye Res.* 2015 Dec;40(12):1261-8. doi: 10.3109/02713683.2014.995310
- Thorne JE, Sugar EA, Holbrook JT, Burke AE, Altaweel MM, Vitale AT, et al. Periocular triamcinolone vs. intravitreal triamcinolone vs. intravitreal dexamethasone implant for the treatment of uveitic macular edema: the POINT trial. *Ophthalmology.* 2019 Feb;126(2):283–95. doi: 10.1016/j.ophtha.2018.08.021.
- Acharya NR, Vitale AT, Sugar EA, Holbrook JT, Burke AE, Thorne JE, et al. Intravitreal therapy for uveitic macular edema ranibizumab versus methotrexate versus the dexamethasone implant: the MERIT trial results. *Ophthalmology.* 2023 Sep;130(9):914–23. doi: 10.1016/j.ophtha.2023.04.011.
- Patil NS, Mihalache A, Hatamnejad A, Popovic MM, Kertes PJ, Muni RH. Intravitreal steroids compared with anti-VEGF treatment for diabetic macular edema: a meta-analysis. *Ophthalmol Retina.* 2023 Apr;7(4):289–99. doi: 10.1016/j.oret.2022.10.008.
- He Y, Ren XJ, Hu BJ, Lam WC, Li XR. A meta-analysis of the effect of a dexamethasone intravitreal implant versus intravitreal anti-vascular endothelial growth factor treatment for diabetic macular edema. *BMC Ophthalmol.* 2018 May;18(1):121. doi: 10.1186/s12886-018-0779-1.
- Sharma A, Bellala K, Dongre P, Reddy P. Anti-VEGF versus dexamethasone implant (Ozurdex) for the management of centre-involved diabetic macular edema (CiDME): a randomized study. *Int Ophthalmol.* 2020 Jan;40(1):67–72. doi: 10.1007/s10792-019-01151-3.
- Qian T, Zhao M, Xu X. Comparison between anti-VEGF therapy and corticosteroid or laser therapy for macular oedema secondary to retinal vein occlusion: a meta-analysis. *J Clin Pharm Ther.* 2017 Oct;42(5):519–29. doi: 10.1111/jcpt.12551.
- Zhang W, Liu Y, Sang A. Efficacy and effectiveness of anti-VEGF or steroids monotherapy versus combination treatment for macular edema secondary to retinal vein occlusion: a systematic review and meta-analysis. *BMC Ophthalmol.* 2022 Dec;22(1):472. doi: 10.1186/s12886-022-02682-7.
- Lin Y, Ren X, Chen D. Steroid treatment in macular edema: a bibliometric study and visualization analysis. *Front Pharmacol.* 2022 Feb 22;13:824790. doi: 10.3389/fphar.2022.824790.
- Levin MH, Pistilli M, Daniel E, Gangaputra SS, Nussenblatt RB, Rosenbaum JT, et al. Incidence of visual improvement in uveitis cases with visual impairment caused by macular edema. *Ophthalmology.* 2014 Feb;121(2):588–595.e1.
- Invernizzi A, Pichi F, Symes R, Zagora S, Agarwal AK, Nguyen P, et al. Twenty-four-month outcomes of inflammatory choroidal neovascularisation treated with intravitreal anti-vascular endothelial growth factors: a comparison between two treatment regimens. *Br J Ophthalmol.* 2020 Aug;104(8):1052–6. doi: 10.1136/bjophthalmol-2019-315257.

15. Cheng ZA, Liu X. Comparing the efficacy of glucocorticoids and anti-VEGF in treating diabetic macular edema: systematic review and comprehensive analysis. *Front Endocrinol.* 2024 Mar 22;15:1342530. doi: 10.3389/fendo.2024.1342530.
16. Koc H, Alpay A, Ugurbas SH. Comparison of the efficacy of intravitreal anti-VEGF versus intravitreal dexamethasone implant in treatment resistant diabetic macular edema. *BMC Ophthalmol.* 2023 Mar 13;23(1):97. doi: 10.1186/s12886-023-02831-6.
17. Kelkar A, Kelkar J, Dutta S, Bolisetty M, Jain H, Labhsetwar N. Management of coexisting cataract and diabetic macular edema: a comparative study of dexamethasone implant versus anti-VEGF agents injections. *Int J Ophthalmol.* 2026 Jan;19(1):56-62. doi: 10.18240/ijo.2026.01.07.
18. Zabaneh ID, Dunn T, Dunn K, Williams P. Comparative incidence of endophthalmitis after intravitreal dexamethasone implant versus anti-VEGF injections: a retrospective study. *Int J Retina Vitreous.* 2026 Feb 23;12(1):50. doi: 10.1186/s40942-026-00824-3.
19. Maturi RK, Bleau L, Saunders J, Mubasher M, Stewart MW. A 12-month, single-masked, randomized controlled study of eyes with persistent diabetic macular edema after multiple anti-VEGF injections to assess the efficacy of the dexamethasone-delayed delivery system as an adjunct to bevacizumab compared with continued bevacizumab monotherapy. *Retina.* 2015 Aug;35(8):1604–14. doi: 10.1097/IAE.0000000000000533.
20. Lee JY, Lee SY, Kim JY, Lee HJ, Jeong JH, Ma DJ. Effect of alternate treatment with intravitreal anti-vascular endothelial growth factor and steroid for treatment-naïve diabetic macular edema in a real-life setting. *J Ocul Pharmacol Ther.* 2020 Sep;36(7):555–62. doi: 10.1089/jop.2020.0012.
21. Cai X, Zhao J, Dang Y. Combination therapy with anti-VEGF and intravitreal dexamethasone implant for macular edema secondary to retinal vein occlusion. *Curr Eye Res.* 2024 Aug;49(8):872–8. doi: 10.1080/02713683.2024.2343055.
22. Bae YH, Kim SM, Kim JY, Bae SH, Kim H, Ma DJ. Effect of alternate treatment with intravitreal corticosteroid and anti-VEGF for macular edema secondary to retinal vein occlusion. *J Ophthalmol.* 2021;2021:5948113. doi: 10.1155/2021/5948113.
23. Cui BH, Zhou W, Wang WW, Yang H, Dong YL, Liu YY, et al. Clinical efficacy of intravitreal corticoid as an adjunctive therapy to anti-VEGF treatment of neovascular age-related macular degeneration: a meta-analysis. *Int J Ophthalmol.* 2021 Jul 18;14(7):1092-9. doi: 10.18240/ijo.2021.07.19.
24. Kaya C, Zandi S, Pfister IB, Gerhardt C, Garweg JG. Adding a corticosteroid or switching to another anti-VEGF in insufficiently responsive wet age-related macular degeneration. *Clin Ophthalmol.* 2019 Dec;13:2403–9. doi: 10.2147/OPTH.S224456.
25. Kumar A, Kumar A, Kumar J, Bai G, Jeewnani R, Dembra M, et al. Comparative efficacy of anti-vascular endothelial growth factor (anti-VEGF) agents and corticosteroids in managing diabetic retinopathy-associated diabetic macular edema: a meta-analysis and comprehensive systematic review. *Cureus.* 2024 Jan 8;16(1) :e51910. doi: 10.7759/cureus.51910.
26. Naz U, Naz S, Rizvi F, Kamil Z. Pattern of uveitis in a tertiary care eye hospital setting in Pakistan: a comprehensive analysis. *Ocul Immunol Inflamm.* 2025 Sep;33(7):1108–1112. doi: 10.1080/09273948.2024.2439903.
27. Putera I, Thiadens AAHJ, Larasmanah ASN, La Distia Nora R, Dik WA, van Hagen PM, Rombach SM, Ten Berge JCEM. Uveitic macular oedema in ocular tuberculosis patients in a non-endemic country: characteristics, management, and visual outcomes. *Eye (Lond).* 2025 Feb;39(3):593–601. doi: 10.1038/s41433-024-03577-1.