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Original Research Paper

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# A PROSPECTIVE CLINICO-COMPARATIVE EVALUATION OF VARIOUS ANTI-VASCULAR ENDOTHELIAL GROWTH FACTORS IN VARIOUS RETINAL DISORDERS

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## ABSTRACT

**Background:** Retinal disorders are major causes of visual impairment, particularly in elderly individuals and those with diabetes and hypertension. VEGF plays a central role in macular oedema and retinal/choroidal neovascularisation. This study compared the effectiveness and safety of commonly used intravitreal anti-VEGF agents. **Materials and Methods:** A prospective observational clinico-comparative study was conducted at Netaji Subhash Chandra Bose Medical College and Hospital, Jabalpur, over one year. Patients aged ≥40 years with diabetic macular oedema (DME), choroidal neovascularisation (CNVM), retinal vein occlusion-related macular oedema (RVO-ME), or age-related macular degeneration (AMD) received bevacizumab, ranibizumab, or aflibercept. BCVA and central macular thickness (CMT) were assessed at baseline and during follow-up. **Results:** DME was most common (38%), followed by CNVM (26%), RVO-ME (20%), and AMD (16%). Mean BCVA improved from 0.92 ± 0.28 to 0.48 ± 0.22 logMAR, while CMT decreased from 452 ± 96 to 298 ± 72 $\mu$m at 3 months ($p<0.001$). Aflibercept showed relatively greater improvement. No complications occurred in 85%; subconjunctival haemorrhage occurred in 10% and transient IOP elevation in 5%. **Conclusion:** Intravitreal anti-VEGF therapy significantly improved visual and anatomical outcomes with a favourable safety profile.

**KEYWORDS :** Anti-Vegf; Bevacizumab; Ranibizumab; Aflibercept; Diabetic Macular Oedema; Choroidal Neovascularisation; Retinal Vein Occlusion; Age-Related Macular Degeneration; Visual Acuity; Central Macular Thickness

## INTRODUCTION

Retinal disorders are major causes of visual impairment, particularly among the elderly and patients with diabetes and hypertension. Increasing life expectancy and metabolic diseases have made retinal vascular disorders an important health concern in India.[1] These include diabetic retinopathy, retinal vein occlusion, and neovascular AMD.[2]

Retinal hypoxia promotes VEGF release, causing vascular permeability, neovascularization, and disruption of the blood-retinal barrier, resulting in macular oedema, haemorrhage, fibrosis, and visual loss.[2,3,4]

Diabetic retinopathy causes retinal ischemia and VEGF-mediated leakage leading to diabetic macular oedema (DME).[5] CNVM involves abnormal choroidal vessel growth with leakage and haemorrhage, primarily mediated by VEGF.[6] Retinal vein occlusion causes venous obstruction, non-perfusion, and retinal hypoxia,[7] while neovascular AMD produces VEGF-driven choroidal neovascularization and central visual loss.[8]

VEGF inhibition is therefore central to treatment. Intravitreal anti-VEGF therapy reduces vascular leakage and neovascularization, improving or stabilizing vision.[9] Bevacizumab, ranibizumab, and aflibercept are effective agents, but comparative real-world evidence regarding their effectiveness and safety remains limited.[10]

## MATERIAL AND METHODS

A prospective observational clinico-comparative study was conducted in the Department of Ophthalmology, Netaji Subhash Chandra Bose Medical College and Hospital, Jabalpur, Madhya Pradesh, over a period of one year. Patients attending the ophthalmology outpatient department and retina clinic with retinal disorders requiring intravitreal anti-VEGF therapy were enrolled after Institutional Ethics Committee approval and written informed consent. The minimum calculated sample size was 33 patients.

### Inclusion Criteria

Patients aged ≥40 years, irrespective of gender or race, diagnosed with NPDR, PDR, DME, CNVM, retinal vein occlusion, or AMD were included.

### Exclusion Criteria

Patients aged <40 years, with tractional retinal detachment, uncontrolled hypertension, cerebrovascular infarction, chronic kidney disease, corneal disorders or previous corneal refractive surgery, uveitis, glaucoma, or physical/mental conditions affecting cooperation were excluded.

### Study Procedure

A detailed history was recorded, including demographic characteristics, systemic illnesses, ocular symptoms, previous ocular treatment, and medications. A comprehensive ophthalmic examination was performed before anti-VEGF therapy.

Visual acuity was assessed using a Snellen chart, including unaided and best-corrected visual acuity, pinhole testing, and refraction where applicable. Anterior segment examination was performed using torchlight and slit-lamp biomicroscopy. Adnexal structures and ocular movements were also assessed.

Posterior segment examination was performed after pupillary dilation using direct and indirect ophthalmoscopy and slit-lamp biomicroscopy with a +90D lens. Macular, optic disc, retinal vascular, and peripheral retinal findings were documented.

## OBSERVATION AND RESULTS

**Table 1: Demographic and Clinical Profile of Study Participants (n = 100)**

| Variable | Category | Frequency (n) | Percentage (%) |
|---|---|---|---|
| Age Group | 40–50 years | 22 | 22.0 |
| | 51–60 years | 34 | 34.0 |
| | 61–70 years | 28 | 28.0 |
| | >70 years | 16 | 16.0 |
| Gender | Male | 58 | 58.0 |
| | Female | 42 | 42.0 |
| Retinal Disrder | DME | 38 | 38.0 |
| | CNVM | 26 | 26.0 |
| | RVO-ME | 20 | 20.0 |
| | AMD | 16 | 16.0 |

A total of 100 patients receiving intravitreal anti-VEGF therapy were studied, with most aged 51–60 years (34%) and 61–70 years (28%); 58% were males. DME was the most common disorder (38%), followed by CNVM (26%), RVO-ME (20%), and AMD (16%).

**Table 2: Systemic Risk Factors Among Study Participants**

| Risk Factor | Present (n) | Percentage (%) |
|---|---|---|
| Diabetes Mellitus | 64 | 64.0 |
| Hypertension | 52 | 52.0 |
| Dyslipidaemia | 38 | 38.0 |
| Smoking | 30 | 30.0 |

Diabetes mellitus (64%) and hypertension (52%) were the most common systemic risk factors observed, highlighting their strong association with retinal vascular disorders.

**Table 3: Distribution of Retinal Disorders (n = 100)**

| Retinal Disorder | Frequency (n) | Percentage (%) |
|---|---|---|
| Diabetic Macular Edema (DME) | 38 | 38.0 |
| Choroidal Neovascular Membrane (CNVM) | 26 | 26.0 |
| Retinal Vein -Occlusion with Macular Edema (RVO-ME) | 20 | 20.0 |
| Age-related Macular Degeneration (AMD) | 16 | 16.0 |

Diabetic macular edema (DME) was the most common retinal disorder, accounting for 38% of cases. This was followed by choroidal neovascular membrane (CNVM) in 26% of patients, retinal vein occlusion with macular edema (RVO-ME) in 20%, and age-related macular degeneration (AMD) in 16%.

**Table 4: Visual Outcome Over Time (BCVA)**

| Time Interval | Mean BCVA (logMAR) ± SD |
|---|---|
| Baseline | 0.92 ± 0.28 |
| 1 Week | 0.78 ± 0.26 |
| 1 Month | 0.60 ± 0.24 |
| 3 Months | 0.48 ± 0.22 |

**Statistical Analysis**

**Repeated Measures ANOVA**

F-value: $F(3,297) = 142.3$, $p < 0.001$

A progressive and statistically significant improvement in visual acuity was observed over time. Mean BCVA improved from 0.92 ± 0.28 logMAR at baseline to 0.48 ± 0.22 logMAR at 3 months ($p < 0.001$), indicating substantial functional recovery following anti-VEGF therapy.

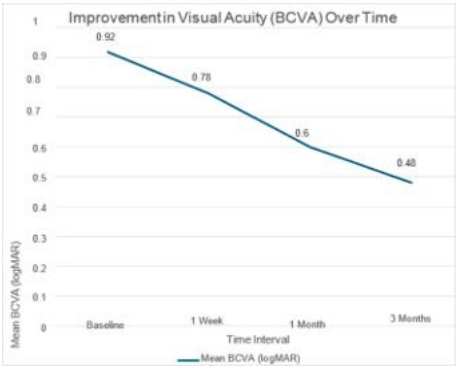


**Figure 1: Change in Best-corrected Visual Acuity (BCVA) Over Time Following Anti-VEGF Therapy**

**Table 5: Anatomical Outcome Over Time (CMT) Change in Central Macular Thickness (CMT) Over Time Following Anti-VEGF Therapy**

| Time Interval | Mean CMT (μm) ± SD |
|---|---|
| Baseline | 452 ± 96 |
| 1 Month | 320 ± 78 |
| 3 Months | 298 ± 72 |

**Statistical Test Applied:**

Overall test: Repeated Measures ANOVA F-value: $F(2,198) = 168.7$, $p < 0.001$.

A significant reduction in central macular thickness was noted, decreasing from 452 ± 96 μm at baseline to 298 ± 72 μm at 3 months ($p < 0.001$), reflecting a strong anatomical response to treatment.

**Table 6: Baseline Ocular Profile and Anti-VEGF Agents Used (n = 100)**

| Variable | Category | Frequency (n) | Percentage (%) |
|---|---|---|---|
| Baseline BCVA | <6/60 | 30 | 30.0 |
| | 6/60–6/36 | 40 | 40.0 |
| | 6/36–6/18 | 20 | 20.0 |
| | >6/18 | 10 | 10.0 |
| Anti-VEGF Agent | Bevacizumab | 46 | 46.0 |
| | Ranibizumab | 32 | 32.0 |
| | Aflibercept | 22 | 22.0 |

At baseline, most patients had moderate visual impairment, with 40% having BCVA between 6/60–6/36 and 30% having BCVA <6/60. Bevacizumab (46%) was the most commonly used anti-VEGF agent, followed by ranibizumab (32%) and aflibercept (22%), reflecting its wider availability and cost-effectiveness in clinical practice.

**Table 7: Disease-wise Comparison of Visual Acuity (BCVA) Before and After Treatment**

| Retinal Disorder | Pre-treatment BCVA (logMAR) ± SD | Post-treatment BCVA (logMAR) ± SD | t-value | p-value |
|---|---|---|---|---|
| DME | 0.95 ± 0.26 | 0.62 ± 0.23 | 7.85 | <0.001 |
| CNVM | 0.90 ± 0.25 | 0.44 ± 0.18 | 9.12 | <0.001 |
| RVO-ME | 0.93 ± 0.27 | 0.52 ± 0.22 | 8.34 | <0.001 |
| AMD | 0.88 ± 0.24 | 0.40 ± 0.17 | 9.67 | <0.001 |

Statistical test applied: Paired t-test.

A highly statistically significant improvement in BCVA was observed across all retinal disorders ($p < 0.001$). The magnitude of visual improvement was greatest in AMD and CNVM, followed by RVO-ME, while DME showed comparatively lesser improvement. This pattern is consistent with the known better functional response of neovascular retinal diseases to anti-VEGF therapy.

**Table 8: Disease-wise Comparison of Central Macular Thickness (CMT) Before and After Treatment**

| Retinal Disorder | Pre-treatment CMT (μm) ± SD | Post-treatment CMT (μm) ± SD | t-value | p-value |
|---|---|---|---|---|
| DME | 470 ± 90 | 325 ± 75 | t = 9.24 | p < 0.001 |
| CNVM | 440 ± 85 | 295 ± 65 | t = 8.91 | p < 0.001 |
| RVO-ME | 455 ± 88 | 290 ± 68 | t = 9.67 | p < 0.001 |
| AMD | 430 ± 80 | 300 ± 60 | t = 8.45 | p < 0.001 |

Statistical test applied: Paired t-test

A significant reduction in central macular thickness (CMT) was observed across all disease groups following treatment ($p < 0.001$), with the greatest reduction seen in DME and RVO-ME, indicating a strong anatomical response to anti-VEGF therapy.

**Drug-wise Comparison of Visual and Anatomical Outcomes**

Paired t-test showed significant improvement in BCVA and reduction in CMT with all three anti-VEGF agents. Aflibercept demonstrated the greatest improvement in BCVA and CMT, followed by ranibizumab and bevacizumab, suggesting a comparatively better anatomical and functional response with aflibercept.

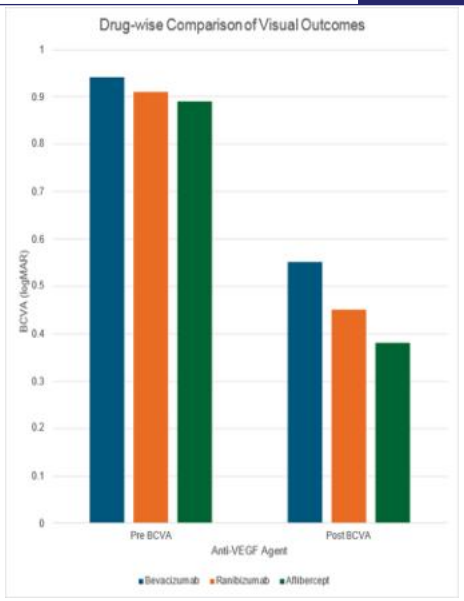


**Figure 2: Comparison of Visual Outcomes (BCVA) Among Different anti-VEGF Agents**

**Table 9: Complications Observed Following Intravitreal Anti-VEGF Injection (n = 100)**

| Complication | Frequency (n) | Percentage (%) |
|---|---|---|
| No complications | 85 | 85.0 |
| Subconjunctival hemorrhage | 10 | 10.0 |
| Raised intraocular pressure | 5 | 5.0 |
| Total | 100 | 100.0 |

The majority of patients (85%) did not experience any complications following intravitreal injection. Minor complications included subconjunctival hemorrhage (10%) and transient rise in intraocular pressure (5%), which were self-limiting. No serious adverse events were observed, indicating that intravitreal anti-VEGF therapy is a safe treatment modality.

**Table 10: Detailed Distribution and Outcome of Complications Following Intravitreal Anti-VEGF Injection (n = 100)**

| Complication | Frequency (n) | Percentage (%) | Time of Occurrence | Management | Outcome |
|---|---|---|---|---|---|
| No Complications | 85 | 85.0 | — | — | — |
| Subconjunctival hemorrhage | 10 | 10.0 | Immediate | No treatment required | Resolved |
| Raised intraocular Pressure | 5 | 5.0 | Within 24 hours | Topical anti-glaucoma drugs | Resolved |
| Endophthalmitis | 0 | 0 | — | — | — |
| Retinal detachment | 0 | 0 | — | — | — |
| Systemic adverse events | 0 | 0 | — | — | — |
| Total | 100 | 100.0 | — | — | — |

Intravitreal anti-VEGF therapy showed a favourable safety profile, with 85% of patients experiencing no complications.

Subconjunctival haemorrhage occurred in 10% and transient IOP elevation in 5%, both resolving with appropriate management. No endophthalmitis, retinal detachment, or systemic adverse events were observed, supporting the overall safety and tolerability of the therapy.

**Table 11: Disease-wise Ocular Findings Among Study Participants**

| Retinal Disorder | Macular Edema (n, %) | Hemorrhages (n, %) | Hard Exudates (n, %) |
|---|---|---|---|
| DME (n=38) | 38 (100.0) | 18 (47.4) | 26 (68.4) |
| CNVM (n=26) | 20 (76.9) | 16 (61.5) | 6 (23.1) |
| RVO-ME (n=20) | 20 (100.0) | 15 (75.0) | 8 (40.0) |
| AMD (n=16) | 10 (62.5) | 5 (31.3) | 3 (18.8) |

Macular oedema was present in all DME and RVO-ME cases but was less frequent in CNVM and AMD. Haemorrhages were common in RVO-ME (75.0%) and CNVM (61.5%), while hard exudates predominated in DME (68.4%), demonstrating distinct ocular profiles across retinal disorders.

## DISCUSSION

In the present study, most patients were aged 51–60 years (34%), followed by 61–70 years (28%), indicating a predominance of retinal disorders among middle-aged and elderly individuals. Khandelwal et al. (2024) reported similar findings, while Wells et al. (2016) observed higher DME prevalence with increasing age and diabetes duration.[11,12] Raman R et al. (2016) reported a younger diabetic retinopathy population in India, possibly reflecting earlier disease onset and greater metabolic burden.[13] Chronic hyperglycaemia, hypertension, and dyslipidaemia contribute to endothelial dysfunction and increased VEGF expression.[1,14]

Males constituted 58% and females 42%, consistent with Khandelwal et al. and Wells et al.[11,12] However, Wong TY et al. and the Beaver Dam Eye Study reported similar disease occurrence between sexes.[1,5] The observed male predominance may therefore reflect healthcare access and health-seeking behaviour.

DME was the commonest disorder (38%), followed by CNVM (26%), RVO-ME (20%), and AMD (16%). Similar findings were reported by Khandelwal et al., while Pham et al. identified DME and RVO as major anti-VEGF indications.[11,15] The lower AMD proportion may reflect the greater burden of diabetes-related retinal disease in India.[1,13]

BCVA improved significantly from 0.92 ± 0.28 to 0.48 ± 0.22 logMAR at 3 months ($p<0.001$), consistent with Wells et al., Martin DF et al., and Khandelwal et al.[12,16,11] This improvement may result from reduced VEGF-mediated permeability and resolution of macular oedema.[3,4,14]

CMT decreased from 452 ± 96 to 298 ± 72 $\mu$m ($p<0.001$), similar to findings by Khandelwal et al., Pham et al., and COPERNICUS.[11,15,17] Anatomical improvement may not always correspond to visual recovery because of chronic retinal damage.[12,16]

All disorders showed significant improvement in BCVA and CMT, with greater visual gain in AMD and CNVM than DME.[12,15] All three agents were effective, with relatively greater improvement with aflibercept, followed by ranibizumab and bevacizumab.[12,15,16] Its apparent advantage may relate to higher VEGF-binding affinity and placental growth factor activity.[19,20] However, observational design and treatment selection bias preclude definitive superiority.

The safety profile was favourable: 85% had no complications, while subconjunctival haemorrhage occurred in 10% and transient IOP elevation in 5%. No endophthalmitis, retinal detachment, or systemic adverse events occurred, consistent with previous reports.[21,22,23]

## CONCLUSION

The overall complication rate was low, and all adverse events

were minor and self-limiting. This confirms the favourable safety profile of intravitreal anti-VEGF injections. Intravitreal anti-VEGF therapy plays a pivotal role in the management of retinal disorders. This leads to significant visual and anatomical improvement. Early diagnosis, timely intervention, and individualised treatment selection are essential for optimising patient outcomes.

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