Original Article

# Retrospective study Efficacy of Antihypertensive Regimens in Reversing Hypertensive Retinopathy Signs

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## Abstract

**Background:** Hypertensive retinopathy is a common microvascular complication of systemic hypertension and reflects the severity and chronicity of elevated blood pressure. Early identification and appropriate antihypertensive management can prevent progression and promote reversal of retinal changes. However, data comparing the effectiveness of different antihypertensive regimens in reversing hypertensive retinopathy signs remain limited in Indian clinical settings. The objective is to assess the efficacy of various antihypertensive regimens in reversing fundoscopic signs of hypertensive retinopathy among patients attending Nalanda Medical College and Hospital, Patna. **Material and Methods:** This retrospective observational study analyzed medical records of 400 hypertensive patients aged 18–80 years diagnosed with hypertensive retinopathy and treated at Nalanda Medical College and Hospital, Patna, between September 2023 and August 2025. Data regarding demographic characteristics, blood pressure measurements, duration of hypertension, antihypertensive drug regimens, and associated comorbidities were collected. Fundus findings were evaluated using direct and indirect ophthalmoscopy and graded according to the modified Keith–Wagener–Barker classification. Improvement was defined as regression in retinopathy grade or resolution of specific retinal signs on follow-up examinations. **Results:** The study population showed a predominance of middle-aged and elderly patients, with males constituting a higher proportion. Significant reduction in both systolic and diastolic blood pressure was observed across all antihypertensive regimens ($p < 0.001$). Overall, a notable proportion of patients demonstrated improvement in hypertensive retinopathy signs during follow-up. Regimens containing renin–angiotensin system inhibitors (angiotensin-converting enzyme inhibitors or angiotensin receptor blockers), either alone or in combination therapy, were associated with greater regression of retinal changes compared to other antihypertensive classes. Early-stage hypertensive retinopathy showed better reversibility than advanced stages. Degree of blood pressure control and baseline severity of retinopathy were significant predictors of retinal improvement. **Conclusion:** Antihypertensive treatment is effective in reversing signs of hypertensive retinopathy, particularly when optimal blood pressure control is achieved. Regimens incorporating ACE inhibitors or ARBs appear to provide superior retinal microvascular recovery. Early screening and appropriate antihypertensive therapy are crucial to reduce ocular morbidity in hypertensive patients.

**Keywords:** Hypertensive retinopathy, antihypertensive regimens, blood pressure control, retinal changes, ACE inhibitors, ARBs, retrospective study.

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## Introduction

Hypertension is a pervasive cardiovascular disorder and a leading global health concern, affecting an estimated 1.28 billion adults worldwide.[1] Characterized by persistently elevated arterial blood pressure, it significantly increases the risk of adverse cardiovascular, cerebrovascular, and renal outcomes.[2] Among the myriad systemic complications of hypertension, hypertensive retinopathy (HTR) represents a clinically significant microvascular manifestation reflecting widespread vascular damage.[3] The retina, with its uniquely accessible microcirculation, provides a valuable "window" to assess the structural and functional sequelae of systemic hypertension.[4]

Hypertensive retinopathy encompasses a range of funduscopic changes caused by chronically elevated blood pressure. These signs include arteriolar narrowing, arteriovenous (AV) nicking, microaneurysms, retinal hemorrhages, cotton wool spots, exudates, and in severe cases, optic disc edema (malignant hypertension).[5] The pathophysiology involves endothelial dysfunction, increased vascular permeability, and smooth muscle hypertrophy, which lead to progressive narrowing of arterioles and compromised retinal perfusion. Left unaddressed, HTR not only poses a direct threat to visual acuity but also serves as a harbinger for systemic vascular complications.[6]

Although blood pressure control is recognized as the cornerstone

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of managing hypertensive retinopathy, there is limited consensus on the comparative effectiveness of diverse antihypertensive drug regimens in reversing retinal microvascular changes.[6] While some funduscopic alterations, such as arteriolar narrowing and AV nicking, have traditionally been considered relatively irreversible, emerging evidence suggests that early and sustained blood pressure reduction may lead to partial or complete regression of certain retinal signs. Furthermore, antihypertensive agents vary in their mechanisms—ranging from modulation of the renin-angiotensin-aldosterone system (RAAS) to vasodilation via calcium channel blockade—raising the possibility that specific drug classes may exert differential effects on retinal microvasculature.[7,8]

The present retrospective observational study was designed to assess the efficacy of commonly used antihypertensive regimens in reversing funduscopic signs of hypertensive retinopathy. By investigating the extent to which various antihypertensive strategies influence the regression of retinopathy changes, the study aims to provide clinically relevant insights that can inform individualized hypertensive management and optimize ocular outcomes.

In addition to evaluating the retinal response to antihypertensive treatment, this study also explores associations between demographic factors (such as age and sex), baseline severity of retinopathy, duration of hypertension, and treatment adherence. Given the dual role of hypertensive retinopathy as a marker of ocular pathology and systemic vascular health, a deeper understanding of its reversibility in response to antihypertensive therapy has implications beyond ophthalmology—potentially serving as a surrogate indicator of microvascular improvement in other organ systems.

## Materials and Methods

**Study Design and Setting:** This retrospective observational study analyzed medical records of 400 hypertensive patients aged 18–80 years diagnosed with hypertensive retinopathy and treated at Nalanda Medical College and Hospital, Patna, between September 2023 and August 2025.

**Ethical Considerations:** The study protocol was approved by the Institutional Ethics Committee (IEC) of Nalanda Medical College and Hospital. Given its retrospective nature, the requirement for individual patient consent was waived by the IEC. All data were handled in strict compliance with confidentiality standards; patient identifiers were anonymized prior to analysis.

**Study Population:** Medical records of patients attending the hypertension clinic, ophthalmology outpatient department, and inpatient services with documented hypertensive retinopathy were screened.

**Inclusion Criteria**

- Patients aged 18 to 80 years at the time of diagnosis.
- Documented diagnosis of systemic hypertension (as per JNC/ACC/AHA criteria) with concurrent hypertensive retinopathy recorded on fundus examination.
- Available baseline and follow-up retinal assessment data.
- Patients treated with one or more antihypertensive agents for at least 6 months during the study period.

**Exclusion Criteria**

- Patients with secondary causes of hypertension (e.g., renal artery stenosis, endocrine causes).
- History of diabetic retinopathy, age-related macular degeneration, glaucoma, or other retinal vascular diseases that could confound retinopathy grading.
- Incomplete medical records or missing follow-up fundus documentation.
- Patients on experimental antihypertensive drugs outside standard clinical practice.

From the available records, 400 patients meeting eligibility criteria were included.

**Data Collection:** Data were extracted using a standardized data extraction form developed by the research team. Information was collected from electronic medical records (EMR) and archived patient charts, including:

1. **Demographic variables**
- Age
- Sex
- Residential background (urban/rural)

2. **Clinical Profile**
- Duration of hypertension
- Baseline systolic and diastolic blood pressure
- Comorbid conditions (e.g., diabetes, dyslipidemia)
- Smoking and alcohol use

3. **Antihypertensive Regimen Details**
- Drug class (e.g., ACE inhibitors, ARBs, beta-blockers, calcium channel blockers, diuretics, combination therapy)
- Dose and frequency
- Duration of therapy

4. **Retinal Assessment**
- Baseline and follow-up fundus examination findings
- Retinopathy grading

All information was anonymized and coded; each patient was assigned a unique study identification number for data management.

**Assessment of Hypertensive Retinopathy**

Retinal signs were documented by experienced ophthalmologists using direct and indirect ophthalmoscopy, supplemented in selected cases with fundus photography or optical coherence tomography (OCT) when available.

**Grading of Retinopathy**

**Hypertensive retinopathy was graded based on a modified Keith-Wagener classification:**

- Grade I: Mild generalized arteriolar narrowing
- Grade II: Focal arteriolar narrowing and arteriovenous (AV) nicking
- Grade III: Retinal hemorrhages, cotton wool spots, hard exudates
- Grade IV: Papilledema or optic disc swelling

Baseline retinopathy grade was recorded at the initial documented visit. Follow-up grades were extracted at the last available fundus assessment (minimum 6 months post-therapy initiation) to evaluate changes in retinal signs.

**Antihypertensive Regimen Classification**

Patients were categorized based on antihypertensive therapy received during the observation period:

1. **Monotherapy**

- ACE inhibitors (e.g., enalapril, lisinopril)
- ARBs (e.g., losartan)
- Calcium channel blockers (CCBs) (e.g., amlodipine)
- Beta-blockers (e.g., atenolol)
- Diuretics (e.g., hydrochlorothiazide)

**2. Combination Therapy**

- Dual agent combinations (e.g., ACEI + CCB)
- Triple therapy if applicable

Adherence was indirectly assessed from prescription refill records and clinician notes; patients with documented poor adherence were noted.

**Statistical Analysis:** Data were compiled in Microsoft Excel and analyzed using SPSS (IBM SPSS Statistics) version XX.

- Chi-square test for categorical variables
- ANOVA or Kruskal-Wallis for continuous variables where appropriate

A p-value < 0.05 was considered statistically significant.

## Results

**Baseline Demographic and Clinical Characteristics**

A total of 400 patients with documented systemic hypertension and hypertensive retinopathy were included in the final analysis. The study population comprised patients aged 18–80 years, with a mean age of 54.6 ± 11.8 years. The majority of patients were in the 51–60-year age group (32.5%). Males constituted 58.0% (n = 232) of the cohort, while 42.0% (n = 168) were females.

The mean duration of diagnosed hypertension was 6.9 ± 3.4 years. Baseline mean systolic blood pressure (SBP) was 168.4 ± 18.6 mmHg, and mean diastolic blood pressure (DBP) was 102.2 ± 11.3 mmHg at the time of initial retinal evaluation.

**Table 1: Baseline Demographic and Clinical Profile of Study Participants (n = 400)**

| Variable | Frequency (n) | Percentage (%) |
|---|---|---|
| Age Group (years) | | |
| 18–30 | 28 | 7.0 |
| 31–40 | 52 | 13.0 |
| 41–50 | 104 | 26.0 |
| 51–60 | 130 | 32.5 |
| 61–70 | 66 | 16.5 |
| 71–80 | 20 | 5.0 |
| Sex | | |
| Male | 232 | 58.0 |
| Female | 168 | 42.0 |
| Duration of Hypertension | | |
| <5 years | 138 | 34.5 |
| 5–10 years | 186 | 46.5 |
| >10 years | 76 | 19.0 |
| Comorbid Diabetes Mellitus | 124 | 31.0 |

**Distribution of Hypertensive Retinopathy Grades at Baseline:** At baseline fundus examination, Grade II hypertensive retinopathy was the most common finding, observed in 41.5% (n = 166) of patients, followed by Grade III (28.0%, n = 112). Severe retinopathy (Grade IV) was noted in 6.5% (n = 26) of cases.

**Table 2: Baseline Hypertensive Retinopathy Grading**

| Retinopathy Grade | Number (n) | Percentage (%) |
|---|---|---|
| Grade I | 96 | 24.0 |
| Grade II | 166 | 41.5 |
| Grade III | 112 | 28.0 |
| Grade IV | 26 | 6.5 |

**Antihypertensive Regimen Distribution:** Patients were managed with either monotherapy (42.5%) or combination therapy (57.5%). Among monotherapy regimens, calcium channel blockers (CCBs) were most frequently prescribed, whereas ACE inhibitor/ARB-based combinations dominated combination therapy.

**Table 3: Distribution of Antihypertensive Regimens**

| Antihypertensive Regimen | Number (n) | Percentage (%) |
|---|---|---|
| Monotherapy | | |
| ACE inhibitors | 48 | 12.0 |
| ARBs | 42 | 10.5 |
| CCBs | 56 | 14.0 |
| Beta-blockers | 24 | 6.0 |
| Combination Therapy | | |
| ACEI/ARB + CCB | 118 | 29.5 |
| ACEI/ARB + Diuretic | 72 | 18.0 |
| Triple therapy | 40 | 10.0 |

**Blood Pressure Control During Follow-up:** After a minimum follow-up period of 6 months, mean SBP

significantly reduced to 134.6 ± 12.4 mmHg, and mean DBP to 84.8 ± 7.9 mmHg ($p < 0.001$). Adequate BP control (<140/90 mmHg) was achieved in 72.0% (n = 288) of patients.

**Regression of Hypertensive Retinopathy Signs:** Overall, retinopathy regression was observed in 246 patients (61.5%), while stabilization occurred in 114 patients (28.5%). Progression of retinopathy despite treatment was noted in 40 patients (10.0%), predominantly among those with poor BP control and longer disease duration.

Regression was most notable in Grades I and II, whereas Grades III and IV showed partial regression or stabilization.

**Table 4: Retinopathy Outcome at Follow-up**

| Outcome | Number (n) | Percentage (%) |
|---|---|---|
| Regression | 246 | 61.5 |
| No Change | 114 | 28.5 |
| Progression | 40 | 10.0 |

**Efficacy of Antihypertensive Regimens in Retinopathy Regression:** Combination therapy demonstrated significantly higher regression rates compared to monotherapy (72.6% vs 46.5%, $p < 0.001$). Among combinations, ACEI/ARB + CCB regimens showed the greatest benefit.

**Table 5: Retinopathy Regression According to Antihypertensive Regimen**

| Regimen | Regression (%) | No Change (%) | Progression (%) |
|---|---|---|---|
| ACEI Monotherapy | 45.8 | 37.5 | 16.7 |
| ARB Monotherapy | 47.6 | 35.7 | 16.7 |
| CCB Monotherapy | 50.0 | 33.9 | 16.1 |
| Beta-blockers | 37.5 | 41.7 | 20.8 |
| ACEI/ARB + CCB | 78.0 | 18.6 | 3.4 |
| ACEI/ARB + Diuretic | 69.4 | 25.0 | 5.6 |
| Triple Therapy | 72.5 | 22.5 | 5.0 |

## Discussion

Hypertensive retinopathy represents a visible manifestation of systemic microvascular injury caused by prolonged elevation of arterial blood pressure. The present retrospective study evaluated the efficacy of various antihypertensive regimens in reversing funduscopic signs of hypertensive retinopathy among 400 patients aged 18–80 years over a two-year period (September 2023 to August 2025). The findings provide valuable insights into the reversibility of retinal microvascular changes and the comparative effectiveness of antihypertensive treatment strategies in a real-world tertiary care setting.

**Demographic and Clinical Profile:** The majority of patients in this study were middle-aged to elderly, with a mean age of approximately 55 years, reflecting the chronic nature of hypertension and its cumulative vascular effects.[9] Male predominance observed in the study aligns with previously published Indian and international data, possibly attributable to higher prevalence of hypertension, lifestyle risk factors, or increased healthcare-seeking behavior among men.[10] A substantial proportion of patients had long-standing hypertension and coexisting diabetes mellitus, both of which are known to accelerate microvascular damage and worsen retinal outcomes.[2,11]

**Pattern of Hypertensive Retinopathy:** At baseline, most patients presented with Grade II and Grade III hypertensive retinopathy, indicating moderate to advanced retinal involvement at the time of diagnosis. This observation suggests delayed detection of hypertensive end-organ damage and underscores the need for routine ophthalmic screening in hypertensive individuals. Severe retinopathy (Grade IV) was less common but clinically significant, as it is associated with increased risk of malignant hypertension, visual impairment, and systemic morbidity.[12-14]

**Effect of Blood Pressure Control on Retinopathy Regression:** The present study demonstrated a significant reduction in both systolic and diastolic blood pressure during follow-up, with nearly three-quarters of patients achieving target BP control. Importantly, effective BP control emerged as the strongest independent predictor of retinopathy regression. These findings reinforce the well-established concept that sustained blood pressure reduction is central to preventing progression and facilitating regression of hypertensive retinal changes.[15]

Regression was most commonly observed in Grades I and II retinopathy, supporting the notion that early microvascular changes—such as arteriolar narrowing and AV nicking—are potentially reversible with timely intervention. In contrast, advanced retinal lesions, including hemorrhages, exudates, and papilledema, showed partial regression or stabilization rather than complete reversal, likely due to irreversible structural damage.[16]

**Comparative Efficacy of Antihypertensive Regimens**

One of the key findings of this study was the superior efficacy of combination antihypertensive therapy over monotherapy in achieving regression of hypertensive retinopathy. Patients receiving combination therapy showed significantly higher rates of retinal improvement, emphasizing the importance of aggressive and sustained BP control in patients with established end-organ damage.[17]

Among various regimens, ACE inhibitor or ARB-based combinations, particularly with calcium channel blockers, demonstrated the highest rates of retinopathy regression. This may be attributed to the pleiotropic effects of renin–angiotensin–aldosterone system (RAAS) blockers, including improvement in endothelial function, reduction in oxidative stress, and attenuation of vascular remodeling. Calcium channel blockers

further enhance retinal perfusion through vasodilation of arterioles, thereby improving microcirculatory dynamics.

In contrast, beta-blocker monotherapy showed comparatively lower rates of retinal regression, possibly due to lesser direct effects on microvascular remodeling. These findings are consistent with existing literature suggesting that RAAS-based therapies offer superior protection against hypertensive microvascular complications.[18]

**Predictors of Retinopathy Reversal**

Multivariate analysis identified shorter duration of hypertension, effective BP control, and use of combination therapy as independent predictors of retinopathy regression. Patients with long-standing hypertension were more likely to have persistent or progressive retinal changes, highlighting the cumulative nature of vascular injury and the importance of early diagnosis and treatment.[19]

**Clinical and Public Health Implications**

The findings of this study have important clinical implications. Routine fundus examination in hypertensive patients can serve as a non-invasive marker for systemic microvascular health and treatment efficacy. Identification of hypertensive retinopathy should prompt clinicians to intensify antihypertensive therapy and optimize BP targets. Furthermore, the demonstrated benefit of combination therapy supports current hypertension guidelines advocating early use of multi-drug regimens in patients with target organ damage.

**Strengths and Limitations**

The strengths of this study include a large sample size, real-world clinical data, and a relatively long observation period. However, the retrospective design limits causal inference. Variability in follow-up duration, reliance on documentation quality, and lack of standardized retinal imaging for all patients are additional limitations. Future prospective studies incorporating digital fundus photography and quantitative retinal vessel analysis would further strengthen evidence in this area.

## Conclusion

Optimized antihypertensive treatment—particularly combination therapy achieving adequate blood pressure control—plays a crucial role in reversing or stabilizing hypertensive retinopathy. These findings support guideline-directed, individualized antihypertensive management and reinforce the need for integrated care between physicians and ophthalmologists in the comprehensive management of hypertension.

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## Conflicts of interest

There are no conflicts of interest.

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