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RESEARCH ARTICLE
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ASSESSMENT OF RETINAL MICROVASCULAR PHYSIOLOGY IN SYSTEMIC HYPERTENSION: INSIGHTS FROM A TERTIARY CARE CENTRE IN NORTH INDIA

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Abstract

Background: Systemic hypertension induces widespread microvascular alterations that can be non-invasively visualized in the retina. Retinal microcirculation reflects systemic vascular physiology, and hypertensive retinopathy (HR) serves as a marker of target organ damage. Despite the high prevalence of hypertension in India, data correlating physiological and retinal vascular changes from North Indian tertiary centres remain limited.

Objectives: To evaluate and compare retinal microvascular changes among hypertensive and normotensive individuals and to assess the correlation of retinopathy grades with blood pressure levels, duration of hypertension, and associated systemic factors.

Methods: This hospital-based cross-sectional study included 100 hypertensive patients and 100 age- and sex-matched normotensive controls. Detailed systemic and ocular evaluations were performed. Fundus photographs were graded according to the Keith–Wagener–Barker classification. Statistical analysis included t-test, Chi-square, correlation, and logistic regression using SPSS v26.

Results: Retinal microvascular changes were present in 54% of hypertensives versus 10% of controls ($p < 0.001$). Grades I and II hypertensive retinopathy accounted for 48% of cases. Systolic blood pressure and duration of hypertension showed significant correlation with retinopathy grade ($r = 0.41$ and $r = 0.38$, respectively; $p < 0.001$). Coexisting diabetes and dyslipidemia were significantly associated with higher grades of retinopathy ($p < 0.05$). The mean arteriovenous ratio was significantly reduced in hypertensives (0.66 ± 0.06) compared to controls (0.72 ± 0.04).

Conclusion: Retinal microvascular changes are common in hypertensive individuals and closely related to blood pressure severity and duration. The retina serves as a physiological mirror of systemic vascular health, underscoring the importance of regular fundus evaluation in hypertensive management.

Keywords: Hypertension; Retinal microcirculation; Hypertensive retinopathy; Arteriovenous ratio; Fundus photography; Endothelial dysfunction; Microvascular physiology; North India; Blood pressure; Target organ damage.

INTRODUCTION

Hypertension (HTN) is a leading global health concern, affecting over one billion adults and contributing significantly to cardiovascular disease, stroke, kidney disease, and mortality. A silent disease for many, systemic hypertension exerts its deleterious effects particularly on small vessels and capillary beds—areas often less visible yet critical for organ function. Microvascular damage is central to many of its complications.

The retina offers a rare opportunity for direct in vivo observation of the microcirculation. Retinal vessels share embryologic origin, anatomical structure, and regulatory mechanisms (autoregulation, response to metabolic demand) with the microvasculature in brain and kidney. Thus, changes in retinal vessels can serve as a surrogate for systemic microvascular health.

Physiologically, elevated blood pressure increases transmural stress on arterioles. In early stages, this may trigger increased vasomotor tone (vasospasm) and arteriolar constriction to maintain stable perfusion. Chronically, there is remodeling: hypertrophy of vessel walls, thickening of media, hyaline changes, reduced lumen diameter, increased wall-to-lumen ratio (WLR), and sometimes even damage to the endothelium and capillary loss. These changes contribute to increased vascular resistance, reduced perfusion, and ultimately target-organ damage. In the retina, they manifest as generalized or focal arteriolar narrowing, arteriovenous nicking, increased reflection ("copper/silver wiring"), hemorrhages, exudates, cotton-wool spots, and in extreme cases papilledema.

Understanding the link between systemic physiology—blood pressure levels, blood pressure variability or duration, presence of comorbidities such as diabetes, obesity, smoking—and retinal vascular changes can help in risk stratification and early intervention. Moreover, while advanced imaging modalities like OCTA and adaptive optics are providing deeper insight into vessel density and microcapillary perfusion, many ophthalmologic and clinical setups, especially in resource-limited settings, depend on fundus photography and ophthalmoscopic grading. Thus, studies that elucidate fundus-visible microvascular changes in relation to systemic physiological measurements remain highly relevant.

LITERATURE REVIEW

Retinal Vascular Caliber, AV Ratio, and Incident Hypertension

Longitudinal cohort studies have demonstrated that baseline retinal vessel caliber predicts future hypertension. In a meta-analysis of >10,000 individuals without hypertension, narrower retinal arterioles (per 20 μm decrement) were associated with increased odds of developing hypertension (OR ~1.29), and wider venules also conferred risk (OR ~1.14). [1] Similarly, the *Retinal Vessel Caliber and Tortuosity* study with over 9,000 participants showed that narrower arteriolar diameter, wider venular diameter, and smaller arteriole-to-venule ratio (AVR) were associated with higher incidence of hypertension over 5 years. [2]

Physiologically, these caliber changes reflect early microvascular remodeling. A narrower arteriole implies increased vascular resistance, which helps explain associations with elevated systolic BP and pulse pressure. The venular widening may reflect inflammation, endothelial dysfunction, or relative hypoxia downstream. Together, AVR becomes a composite marker of microvascular health.

Cross-Sectional Associations: Hypertension, Arteriolar Narrowing, AV Nicking, Retinopathy Grades

Multiple cross-sectional and population-based studies have documented associations between current hypertension or poor BP control and retinal changes detectable on fundus photography.

- The Atherosclerosis Risk in Communities (ARIC) study showed that generalized arteriolar narrowing was strongly related to current SBP and also to BP measured several years before, in non-diabetic individuals. [3]
- In the *Beaver Dam* study, hypertensive individuals had significantly higher prevalence of arteriolar narrowing, AV nicking, and retinopathy signs compared with normotensive subjects; risk was higher with uncontrolled vs controlled hypertension. [4]

These findings are consistent across different ethnicities and ages. For instance, in adolescents (12-year-olds), higher BP quartiles were associated with narrower arteriolar caliber, even after adjustment for anthropometric confounders. [5]

Indian Studies: Prevalence, Determinants, and Microvascular Findings

In India, several studies have assessed hypertensive retinopathy (HR) prevalence and risk factors, mostly via fundus photography or direct fundoscopy.

- A study in North-Western Karnataka among 300 hypertensive cases found HR prevalence ≈ 49.33%, with Grades I & II being the commonest. Prevalence was significantly higher among those with hypertension duration > 5 years and in older age groups. [6]
- Rajarajeswary et al. (2024) conducted a comparative study of retinal thickness via OCT (though not exactly microvascular caliber) in hypertensives vs normotensives, suggesting structural retinal changes accompany HTN. [7]
- Another Indian study (Ray-Sahu-Naskar et al.) investigated hypertensive retinal changes along with other target-organ damage, showing correlation between HR grades and renal/cardiovascular comorbidities. [8]

However, Indian literature often lacks detailed quantification of retinal vascular caliber, AV ratios, focal narrowing, or systematic comparison with normotensive controls, especially in North India. There's a gap in correlating these fundus-based vascular changes with physiological BP measures (e.g., duration, control), plus comorbidity profile (diabetes, lipids, obesity).

Physiological Mechanisms Underlying Retinal Microvascular Changes in Hypertension

To understand what is observed ophthalmoscopically, physiological mechanisms are crucial:

1. Autoregulation: Retinal blood flow is maintained across a range of systemic BPs via vasoconstriction or dilation of arterioles. Elevated BP causes a chronic shift in this autoregulatory curve, leading to sustained arteriolar constriction.
2. Wall stress and remodeling: High intraluminal pressure causes mechanical stress on vessel walls. Smooth muscle hypertrophy, deposition of extracellular matrix, thickening of basement membrane, and hyaline changes reduce lumen diameter and elasticity.
3. Endothelial dysfunction: Shear stress, oxidative stress, and inflammation in hypertension impair endothelial function, reduce nitric oxide, promote vasoconstrictor factors, increasing arteriolar tone and vascular permeability. Endothelial damage also contributes to leakage (hemorrhages, exudates) and ischemic areas (cotton-wool spots).
4. Capillary rarefaction: Loss of capillaries (functional or structural) reduces microvascular density, increasing resistance; while beyond direct visible signs, changes in vascular caliber may reflect this process.
5. Interaction with comorbidities: Conditions such as diabetes, dyslipidemia, obesity, smoking compound vascular injury – hyperglycemia induces non-enzymatic glycation, oxidative stress; dyslipidemia affects lipid deposition and vessel wall thickening; obesity increases systemic inflammation.

METHODOLOGY

Study Title

Assessment of Retinal Microvascular Physiology in Systemic Hypertension: Insights from A Tertiary Care Centre in North India

Study Design

Hospital-based, cross-sectional comparative study involving hypertensive patients and age- and sex-matched normotensive controls.

Study Setting and Duration
The study was conducted jointly by the Departments of Ophthalmology and Physiology at a tertiary care teaching hospital in North India over 12 months (August 2020-July 2021).

AIMS AND OBJECTIVES

Primary Objective:
- To assess and compare retinal microvascular changes in patients with systemic hypertension and normotensive controls using fundus photography.

Secondary Objectives:
- To correlate grades of hypertensive retinopathy with levels and duration of blood pressure.
- To study the association between severity of hypertension and systemic factors (age, diabetes, dyslipidemia, smoking) with retinal vascular changes.

INCLUSION CRITERIA

Hypertensive Group
- Adults aged 30–75 years.
- Diagnosed cases of systemic hypertension (as per JNC 8 criteria or on antihypertensive therapy).
- Willing to provide informed written consent.

Control Group
- Age- and sex-matched normotensive individuals (BP <130/85 mmHg).
- No history of hypertension or systemic illness affecting retinal vasculature.
- Willing to participate and provide consent.

EXCLUSION CRITERIA (applied to both groups)
- History of retinal vascular occlusion, diabetic retinopathy, or glaucoma.
- High myopia (> ±6 diopters) or significant media opacity obscuring fundus view.
- Previous intraocular surgery (except uncomplicated cataract surgery >6 months earlier).
- Systemic vasculitis or connective tissue disease.
- Pregnancy or lactation.
- Poor-quality fundus images precluding grading.

Sample Size and Sampling Technique
Assuming a moderate correlation (r = 0.3) between systolic blood pressure and hypertensive retinopathy grade, with 80% power and 5% α-error, the minimum required sample size was 85 subjects per group.
To account for image exclusions or attrition, 100 hypertensive patients and 100 normotensive controls (total **n = 200**) were enrolled using consecutive sampling from outpatient clinics.

Data Collection Procedure
1. Enrollment and Consent:
Eligible subjects were briefed and written informed consent obtained.
2. Clinical and Demographic Data:
Age, sex, occupation, duration of hypertension, current medications, associated comorbidities (diabetes, dyslipidemia, smoking, alcohol), and family history of cardiovascular disease were recorded.
3. Systemic Evaluation:
- Blood Pressure: Measured using a calibrated sphygmomanometer after 5 minutes of rest in a seated position. Two readings 5 minutes apart were averaged.

- BMI: Calculated from measured height and weight.
- Laboratory Tests: Fasting blood sugar/HbA1c, lipid profile, and serum creatinine.

4. Ophthalmic Evaluation:
- Visual Acuity: Best-corrected visual acuity with Snellen's chart.
- Slit-Lamp Examination: For anterior segment evaluation.
- Intraocular Pressure: Measured using Goldmann applanation or non-contact tonometer.
- Dilated Fundus Examination: Using 90D lens and indirect ophthalmoscopy.

5. Fundus Photography and Grading:

Fundus photographs centered on the optic disc and macula were taken using a non-mydriatic fundus camera. Images were graded independently by two masked ophthalmologists according to the Keith-Wagener-Barker classification:

Grade	Description **(Figure 1)**
I	Mild generalized arteriolar narrowing
II	More severe narrowing and focal constrictions
III	Hemorrhages, hard exudates, or cotton-wool spots
IV	Grade III changes with papilledema

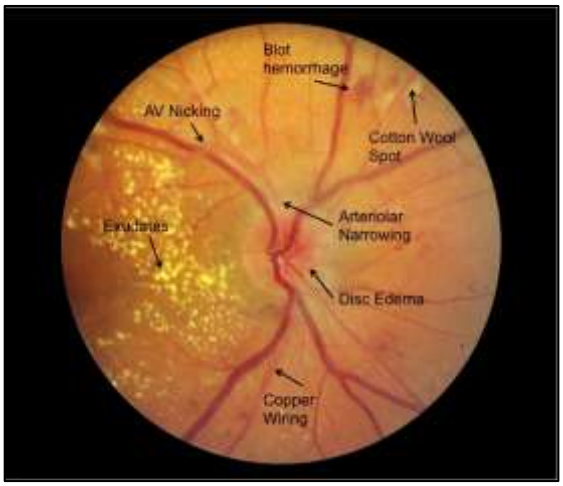

Figure 1 Hypertensive Retinopathy (Classical Findings).

Disagreements were resolved by consensus. Interobserver agreement was assessed using Cohen's kappa coefficient.

Statistical Analysis

Data were analyzed using SPSS v26. Continuous variables were expressed as mean ± SD; categorical variables as frequency (%).

Comparisons between groups used Student's *t*-test and Chi-square test. Correlations were tested using Pearson's coefficient, and multivariate logistic regression was used to assess predictors of retinopathy. A p value < 0.05 was considered statistically significant.

RESULTS

1. **Baseline Demographic and Clinical Characteristics**

Parameter	Hypertensive (n=100)	Control (n=100)	p-value
Age (years, mean ± SD)	54.6 ± 10.8	52.9 ± 9.7	0.28
Male : Female ratio	56 : 44	54 : 46	0.79
BMI (kg/m², mean ± SD)	26.3 ± 3.8	25.1 ± 3.6	0.07
Systolic BP (mmHg)	148.4 ± 14.6	122.3 ± 8.5	<0.001

Diastolic BP (mmHg)	91.2 ± 8.7	77.1 ± 6.4	<0.001
Duration of HTN (years, mean ± SD)	7.2 ± 5.1	—	—
Diabetes mellitus	26 (26%)	8 (8%)	0.002
Dyslipidemia	22 (22%)	10 (10%)	0.03
Smokers	24 (24%)	15 (15%)	0.12

2. **Prevalence and Grades of Hypertensive Retinopathy**

Keith–Wagener–Barker Grade	Hypertensive (n=100)	Controls (n=100)
No retinopathy	46 (46%)	90 (90%)
Grade I	30 (30%)	10 (10%)
Grade II	18 (18%)	0
Grade III	5 (5%)	0
Grade IV	1 (1%)	0
Total with changes	54 (54%)	10 (10%)

Grade I, II, III and IV Retinopathy was seen in 30%, 18%, 5% and 1% Hypertensive patients Respectively with No Retinopathy observed in 46% Hypertensives. (**Figure 2 and 3**).
Overall prevalence of hypertensive retinopathy among hypertensives was 54%, predominantly Grades I–II.

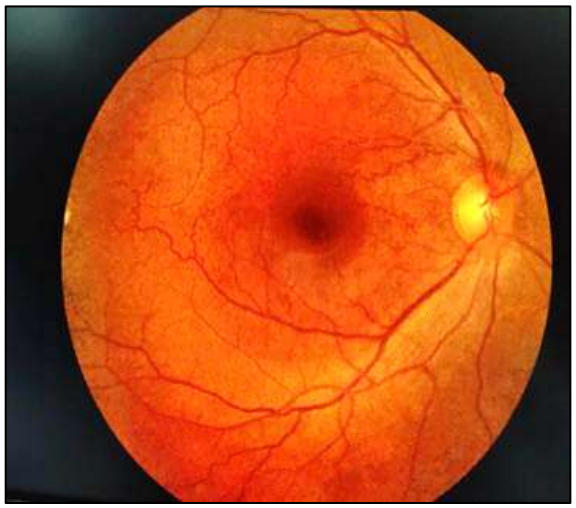

Figure 2 Right Eye Fundus photograph showing Grade 2 Hypertensive Retinopathy

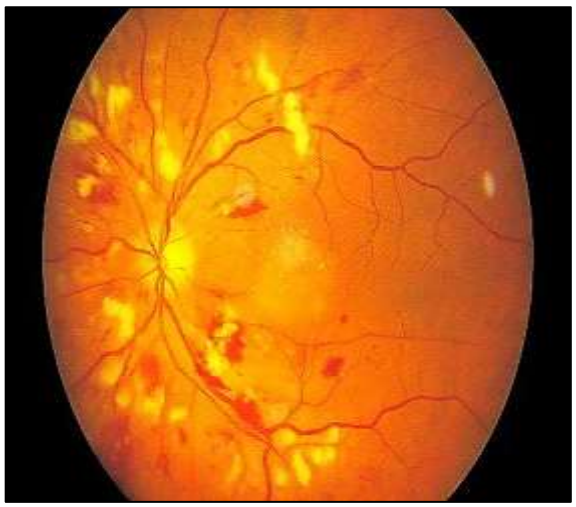

Figure 3 Left Eye Fundus photograph showing Grade 4 Hypertensive Retinopathy

3. **Correlation Between Retinopathy and Blood Pressure / Duration**

Parameter	No Retinopathy (n=46)	Any Retinopathy (n=54)	p-value
Systolic BP (mmHg)	139.8 ± 10.6	154.9 ± 12.7	<0.001
Diastolic BP (mmHg)	88.1 ± 6.3	93.9 ± 8.9	0.002
Duration of HTN (years)	4.3 ± 2.8	9.8 ± 5.2	<0.001

Correlation coefficients:

- Systolic BP vs retinopathy grade: $r = 0.41$, $p < 0.001$
- Duration vs retinopathy grade: $r = 0.38$, $p = 0.001$

4. **Association with Systemic Factors**

Systemic Factor	Retinopathy Present (n, %)	p-value
Diabetes (n=26)	19 (73%)	0.03
Dyslipidemia (n=22)	15 (68%)	0.04
Smoking (n=24)	17 (71%)	0.05
BMI ≥25 kg/m² (n=60)	34 (57%)	0.21

5. **Arteriovenous Ratio Comparison**

Parameter	Hypertensive Group	Control Group	p-value
Arteriovenous ratio (mean ± SD)	0.66 ± 0.06	0.72 ± 0.04	<0.01

A significantly reduced arteriovenous ratio in hypertensives indicates generalized arteriolar narrowing.

DISCUSSION

The present cross-sectional study evaluated retinal microvascular changes in hypertensive individuals compared with normotensive controls using fundus photography. The prevalence of hypertensive retinopathy (HR) in our cohort was 54%, predominantly Grade I and II lesions. These findings closely align with previous Indian and international studies reporting HR prevalence between 45–65% among hypertensive adults [3-6].

Hypertensive retinopathy is an important manifestation of systemic microvascular damage. Persistent elevation of arterial pressure induces arteriolar vasospasm, endothelial dysfunction, and increased vascular wall thickness, resulting in generalized and focal arteriolar narrowing [7,8]. Over time, these physiological responses evolve into structural changes such as arteriovenous crossing (nicking), exudation, and hemorrhage, reflecting increased capillary permeability and breakdown of the blood-retinal barrier [9,10]. Thus, the retina serves as a unique, non-invasive “window” to assess systemic microcirculation.

In our study, the systolic blood pressure showed a significant positive correlation ($r = 0.41$, $p < 0.001$) with retinopathy grade, consistent with findings by Wong et al. [11] and Chatterjee et al. [12], who demonstrated that higher systolic load, rather than diastolic pressure, better predicts microvascular remodeling. The duration of hypertension was also strongly associated with retinopathy severity, supporting the cumulative nature of vascular insult over time [13].

From a physiological standpoint, chronic hypertension causes autoregulatory failure in retinal arterioles. Normally, retinal vessels maintain constant perfusion through myogenic and neurogenic control; however, prolonged hypertension shifts this autoregulatory curve rightward, resulting in increased vascular tone and wall-to-lumen ratio [14]. These mechanisms mirror systemic microvascular changes observed in the kidney and brain, further emphasizing the integrative pathophysiology between cardiovascular and ocular systems [15].

Coexisting metabolic factors such as diabetes, dyslipidemia, and smoking amplified the risk of HR in this study. Diabetic hypertensives showed a 73% prevalence of retinal changes, underscoring the synergistic microangiopathic effects of hyperglycemia and hypertension. Similar associations have

been noted in the Chennai Urban Rural Epidemiology Study (CURES) [16] and the Blue Mountains Eye Study [17]. Dyslipidemia and oxidative stress accelerate endothelial injury, leading to earlier appearance of microaneurysms and flame-shaped hemorrhages [18].

The mean arteriovenous ratio (AVR) was significantly lower among hypertensives (0.66 ± 0.06) compared to controls (0.72 ± 0.04), indicating diffuse arteriolar narrowing. This parameter, which reflects the physiological balance between retinal arteriole and venule calibers, has been validated as a surrogate for systemic vascular resistance and cardiovascular risk [19,20].

The predominance of Grade I–II changes in our population likely reflects better treatment awareness and antihypertensive control, as observed in other hospital-based Indian studies [21]. However, 6% of participants demonstrated Grade III–IV lesions, indicating ongoing end-organ damage despite therapy—emphasizing the need for regular retinal examination in hypertensive patients.

Our findings reinforce the physiological interplay between systemic hemodynamics and retinal microcirculation. Retinal vasculature, lacking autonomic innervation, responds directly to perfusion pressure and local metabolic demand; thus, its alterations mirror systemic vascular injury. Integration of retinal vascular assessment into hypertensive management may serve as an early biomarker of target organ damage.

CONCLUSION

Hypertensive individuals demonstrated a significantly higher prevalence of retinal microvascular alterations compared with normotensive controls. Retinopathy severity correlated strongly with systolic blood pressure and duration of hypertension, while metabolic cofactors such as diabetes and dyslipidemia further accentuated risk.

The study underscores the value of retinal examination as a physiological indicator of systemic vascular health, bridging the disciplines of ophthalmology and cardiovascular physiology. Regular retinal screening, even in asymptomatic hypertensive patients, should be integrated into routine evaluation to identify early microvascular compromise and prevent irreversible end-organ damage.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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