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Original Research Article

The Relationship Between Hypertension and Retinal Microvascular Changes

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Conflict of interest: Nil

Abstract:

Background: Hypertension is a prevalent systemic condition that adversely affects ˙retinal microvasculature, leading to structural and functional changes detectable through advanced imaging. Retinal evaluation provides a non-invasive window into systemic vascular health.

Aim: To assess the impact of chronic and relieved hypertension on retinal microvascular and structural parameters using Optical Coherence Tomography Angiography (OCTA) and standard ophthalmic examinations.

Methodology: This cross-sectional study included 85 eyes from patients with chronic hypertension (n=45), relieved hypertensive retinopathy (n=40), and age-matched healthy controls (n=100). Participants underwent comprehensive ophthalmic evaluation, OCT, and OCTA imaging to measure vessel density (VD), perfusion density (PD), foveal avascular zone (FAZ), central foveal thickness (CFT), ganglion cell-inner plexiform layer (GC-IPL), and retinal nerve ˙fiber layer (RNFL). Data were analyzed using SPSS, with $p < 0.05$ considered significant˙.

Results: Chronic hypertensive participants exhibited significantly reduced VD and PD, enlarged FAZ, and thinner GC-IPL and RNFL compared to controls ($p < 0.01$). Relieved hypertensive participants showed partial improvement in these parameters. Strong correlations were observed between OCTA and structural OCT metrics, indicating a close link between vascular and neuronal retinal changes.

Conclusion: Hypertension induces measurable retinal microvascular and structural alterations, which can be partially reversed with effective blood pressure management. Retinal imaging is a valuable non-invasive tool for early detection of hypertensive end-organ damage.

Keywords: Hypertension, Retinal Microvasculature, OCTA, OCT, Vessel Density, Foveal Avascular Zone.

Introduction

Hypertension (i.e., high blood pressure) is a chronic health condition in which blood pressure in the arteries is chronically high, creating a significant burden on the cardiovascular system as well as other vital organs. It is one of the most prevalent non-communicable diseases worldwide and affects over 1.28 billion adults (30-79 years of age), with many of them either undiagnosed or inadequately controlled [1]. In addition to contributing to cardiovascular morbidity, including myocardial infarction and stroke, hypertension can also have negative outcomes in end-organ systems such as the kidneys, brain, and eyes. Among these organs, the eye is particularly vulnerable due to its unique structural and functional characteristics of microvasculature. The retinal circulation shares the same anatomical and physiological features of the cerebral and renal microvasculature, allowing for an uninvasive assessment of vascular health at a systemic level. Hence, retinal examination is an important part of assessing hypertensive end-organ damage [2].

The retina of the eye is highly sensitive to blood pressure changes. Chronic hypertension may lead to both structural and functional changes in the retinal vasculature such as retinal arteriolar narrowing, arteriovenous nicking, microaneurysm, various hemorrhages, exudates and ultimately, optic disc edema, in the endemic stage. The combination of these changes is referred to as hypertensive retinopathy, which is commonly graded using the Keith-Wagener-Barker classification system or modified Scheie classification system. The clinical significance of recognizing retinal changes early indicates

not only the degree and duration of systemic hypertension but is also positively correlated with increased risk of cardiovascular morbidity and mortality [3]. Additionally, retinal vascular changes may occur before clinical manifestations, ophthalmology exams may serve as a useful tool to identify subclinical end-organ harm in those suffering from hypertension [4].

Recent developments on ophthalmic imaging, such as fundus photography, optical coherence tomography (OCT) and fluorescein angiography have increased the capability to identify minor microvascular alterations in hypertensive patients. Specifically, OCT enables high-resolution cross-sectional retina imaging, allowing accurate retinal nerve fiber layer (RNFL) thickness and other types of structure to be measured [5]. Such modalities have ensured that scholars and practitioners have been able to develop associations on the levels of systemic blood pressure and given certain retinal changes, which has enhanced the stratification of risks and the monitoring of hypertensive patients. Even with these technological advances, the hypertensive retinal changes burden has been high particularly in the low- and middle-income countries with a high prevalence of hypertension, and where access to routine ophthalmic care is limited [6].

The hypertensive retinal changes pathophysiology is multifactorial encompassing the hemodynamic, mechanical and biochemical processes. Constant hypertension leads to endothelial dysfunctions, vascular permeability and vascular remodelling. The mechanisms assist in expanding the retinal arterioles constrictibility, vascular tortuosity, and in the extreme cases retinal ischemia. The presence of hypertension induced oxidative stress and inflammatory factors leading to the microvascular damage and the further weakening of the retinal integrity can also be found [7]. Some of the factors that dictate the extent of retinal involvement are age, years of hypertension, systemic illnesses such as diabetes mellitus and genetic predisposition. To have a clear picture of why hypertensive changes in the retina should be detected and managed early enough is the importance of the knowledge of such mechanisms which at appropriate time would allow one to have a chance that the condition could be reversed before it can cause irreversible visual impairment [8].

The cross-sectional studies that investigate the impact of hypertension on retinal changes present useful epidemiological information regarding the prevalence, trends and severity of hypertensive retinopathy in various people. Through such studies, risk factors to be impacted in relation to retinal involvement can be established and help in developing specific screening and management approaches. Besides, these research studies can guide the health policies of the people to reduce the burden of ocular complications associated with hypertension. Regardless of the increasing evidence, region-specific research is still necessary especially in those populations where hypertension is prevalent and the health care facilities are few and far between to provide baseline information and to inform clinical practice.

The effect of hypertension on retinal structure and activity is significant and the effects are not limited to the health of eyes, as hypertension is a risk factor of the cardiovascular system in general. Non-invasive, accessible and informative mode to identify hypertensive end- organ damage is the retinal examination. Cross-sectional evaluation of hypertensive patients gives essential information on how common and broad retinal changes are, which has been applied in the clinical management as well as preventive approaches. Since hypertension and ocular consequences associated with it continue to increase as a global burden, studies on the impact of hypertension on retinal alterations are necessary to enhance early screening and determine interventional responses to the health issue, and eventually prevent vision-threatening complications.

Methodology

Study Design: This cross-sectional observational study was designed to evaluate the relationship between hypertension and retinal microvascular changes using Optical Coherence Tomography Angiography (OCTA) and standard ophthalmic examinations. The study aimed to compare retinal miczascular parameters in patients with chronic hypertension, patients with relieved hypertensive retinopathy (HTNR), and age-matched healthy controls.

Study Area: The study was conducted at the Department of Ophthalmology, Patna Medical College and Hospital, Patna, Bihar, India for 7 months. All examinations and imaging procedures were performed within the department under standardized conditions.

Study Participants

- **Inclusion Criteria:** Patients without a history of intraocular surgery (except non-complicated cataract surgery), ocular trauma, or other ophthalmic diseases (except grade IV HTNR according to the Keith–Wagener-Barker classification) and without systemic diseases other than hypertension (e.g., diabetes, dyslipidemia, stroke) were included.
- **Exclusion Criteria:** Patients with acute HTNR manifestations (e.g., cotton wool spots, intraretinal hemorrhage, exudative retinal detachment, papilledema), axial length <23.60 mm or >25.55 mm, high astigmatism (>±3 diopters), or best-corrected visual acuity (BCVA) <20/25 were excluded to minimize confounding factors affecting OCTA measurements.

Sample Size

A total of 85 eyes were included in the study. Patients were divided into two primary groups: the chronic hypertension group without HTNR (group A, 45 eyes) and the relieved HTNR group (group B, 40 eyes). Both groups had well-controlled blood pressure at the time of the study. Age-matched healthy controls were also included, with subjects ≥50 years classified as group C (50 eyes) and those <50 years as group D (50 eyes). One eye per participant was randomly selected for analysis.

Procedure: All participants underwent comprehensive ophthalmic evaluation, including measurement of BCVA, spherical equivalent, axial length, and intraocular pressure (IOP) using non-contact tonometry, fundoscopy, and fundus photography. OCT and OCTA imaging were performed using a Cirrus HD-OCT 5000 instrument with AngioPlex software (Carl Zeiss Meditec, Dublin, CA). Prior to imaging, patients received mydriatic drops (tropicamide 5 mg/mL and phenylephrine HCL 5 mg/mL) and anesthetic eye drops (proparacaine hydrochloride 0.5%) to reduce blinking and ensure optimal imaging quality. OCTA scans of the macular area (3 × 3 mm) were obtained twice at a 5-minute interval using FastTrack retinal tracking to minimize motion artifacts. The superficial capillary plexus (SCP) was analyzed, with automatic calculation of vascular density (VD), perfusion density (PD), and foveal avascular zone (FAZ) area. VD and PD were quantified in the 1 mm center, parafoveal inner ring, and 3 mm full macular areas. Central foveal thickness (CFT), ganglion cell-inner plexiform layer thickness (GC-IPL), and retinal nerve fiber layer thickness (RNFL) were measured using standard macular and optic disc cube scan protocols. Image quality was reviewed by two investigators, and scans with signal strength ≤8 or artifacts were excluded.

Statistical Analysis: Demographic and clinical variables including age, sex, BCVA, IOP, axial length, and refractive error were compared between groups using the χ^2 test and Student's t-test. OCT and OCTA parameters (VD, PD, FAZ area, CFT, GC-IPL, RNFL) were analyzed similarly, using the average of two measurements per participant. Linear regression analysis was conducted to assess correlations between OCT and OCTA parameters. All analyses were performed using SPSS for Windows (version 27.0, SPSS), with continuous variables presented as mean ± standard deviation. Snellen BCVA was converted to logMAR values, and a p-value <0.05 was considered statistically significant.

Result

Table 1 presents the demographic and clinical characteristics of the study participants across four groups. The mean age differed significantly among groups, with Group A (chronic hypertension) and Group C (control ≥50 years) having higher mean ages of 60.6 ± 6.7 and 61.2 ± 5.9 years, respectively, compared to Group B (relieved HTN, 41.9 ± 8.8) and Group D (control <50 years, 42.3 ± 7.4) ($p < 0.001$). Gender distribution was similar across all groups ($p = 0.85$). Best-corrected visual acuity (BCVA), intraocular pressure (IOP), axial length, and spherical equivalent showed no statistically significant differences between the groups, with mean BCVA ranging from 0.06 to 0.09 logMAR, IOP from 15.2 to 16.2 mmHg, axial length from 24.0 to 24.2 mm, and spherical equivalent from +0.15 to +0.30 D. Overall, apart from age, the groups were comparable in terms of ocular parameters and gender distribution.

Table 1: Demographic and Clinical Characteristics of Study Participants

Parameter	Group A (Chronic HTN, n=45)	Group B (Relieved HTNR, n=40)	Group C (Control ≥50 yrs, n=50)	Group D (Control <50 yrs, n=50)	p-value
Age (years, mean ± SD)	60.6 ± 6.7	41.9 ± 8.8	61.2 ± 5.9	42.3 ± 7.4	<0.001
Sex (M/F)	25/20	22/18	28/22	26/24	0.85
BCVA (logMAR, mean ± SD)	0.08 ± 0.03	0.09 ± 0.04	0.07 ± 0.02	0.06 ± 0.02	0.12
IOP (mmHg, mean ± SD)	16.2 ± 2.1	15.8 ± 2.0	15.5 ± 1.8	15.2 ± 1.7	0.08
Axial length (mm, mean ± SD)	24.1 ± 0.9	24.0 ± 1.0	24.2 ± 0.8	24.1 ± 0.7	0.65
Spherical equivalent (D, mean ± SD)	+0.25 ± 1.1	+0.30 ± 1.0	+0.20 ± 0.9	+0.15 ± 1.0	0.72

Table 2 presents the OCTA parameters, including vessel density (VD) and perfusion density (PD), across different macular regions in four study groups. There is a progressive increase in both VD and PD from Group A to Group D in all assessed areas, with Group D showing the highest values in the 1 mm central region, inner ring, and 3 mm full macula. Specifically, VD increased from 18.5 ± 1.2 mm/mm² in Group A to 20.3 ± 1.0 mm/mm² in Group D at the 1 mm center, while PD similarly rose from 42.3 ± 2.5% to 44.8 ± 2.1%. The inner ring and 3 mm full macular measurements followed the same trend. All differences among the groups were statistically significant ($p < 0.01$), indicating a clear variation in macular vascular parameters between the groups.

Table 2: OCTA Parameters (VD and PD) in Different Macular Areas					
Parameter	**Group A (n=45)**	**Group B (n=40)**	**Group C (n=50)**	**Group D (n=50)**	**p-value**
VD 1 mm center (mm/mm²)	18.5 ± 1.2	19.2 ± 1.1	20.1 ± 1.0	20.3 ± 1.0	<0.01
VD inner ring	17.8 ± 1.3	18.6 ± 1.2	19.5 ± 1.1	19.7 ± 1.0	<0.01
VD 3 mm full	18.1 ± 1.2	18.9 ± 1.1	19.8 ± 1.0	20.0 ± 0.9	<0.01
PD 1 mm center (%)	42.3 ± 2.5	43.1 ± 2.4	44.5 ± 2.0	44.8 ± 2.1	<0.01
PD inner ring (%)	41.8 ± 2.6	42.6 ± 2.3	43.9 ± 2.1	44.2 ± 2.0	<0.01
PD 3 mm full (%)	42.0 ± 2.4	42.8 ± 2.2	44.1 ± 2.0	44.4 ± 1.9	<0.01

Table 3 shows the comparison of Foveal Avascular Zone (FAZ) area and retinal thickness parameters among four groups. The FAZ area was highest in Group A (0.32 ± 0.04 mm²) and progressively decreased across Groups B (0.30 ± 0.03 mm²), C (0.28 ± 0.03 mm²), and D (0.27 ± 0.02 mm²), with a statistically significant difference ($p < 0.01$). Similarly, central foveal thickness (CFT) increased from Group A (243 ± 12 µm) to Group D (260 ± 9 µm), GC-IPL thickness rose from 76 ± 5 µm in Group A to 83 ± 4 µm in Group D, and RNFL thickness increased from 92 ± 8 µm to 101 ± 5 µm across the groups, all showing significant differences ($p < 0.01$). These findings indicate a clear trend of decreasing FAZ area with concomitant increase in retinal thickness parameters from Group A to D.

Table 3: Foveal Avascular Zone (FAZ) Area and Retinal Thickness Parameters					
Parameter	**Group A (n=45)**	**Group B (n=40)**	**Group C (n=50)**	**Group D (n=50)**	**p-value**
FAZ area (mm²)	0.32 ± 0.04	0.30 ± 0.03	0.28 ± 0.03	0.27 ± 0.02	<0.01
Central foveal thickness (CFT, µm)	243 ± 12	250 ± 11	258 ± 10	260 ± 9	<0.01
GC-IPL thickness (µm)	76 ± 5	78 ± 6	82 ± 5	83 ± 4	<0.01
RNFL thickness (µm)	92 ± 8	95 ± 7	100 ± 6	101 ± 5	<0.01

In Table 4, OCT and OCTA parameters are compared between study groups to show significant differences in retinal and vascular parameters by group. Group A had a significantly lower vessel density (VD) at the 1 mm center, and perfusion density (PD) in the inner ring, which showed a mean difference of -1.6 and -2.1, respectively ($p < 0.01$). In Group B, VD was reduced in the 3 mm full area and mean foveal avascular zone (FAZ) was increased when compared to Group D, with mean differences of -1.1 and 0.03, respectively ($p = 0.02$ and 0.01). Group A also had a lower ganglion cell-inner plexiform layer (GC-IPL) thickness and retinal nerve fiber layer (RNFL) thickness compared to Group B, which showed mean differences of -2 and -3, respectively ($p = 0.04$ and 0.03). These values reflect measurable structural and vascular differences between groups.

Table 4: Comparison of OCT/OCTA Parameters Between Groups			
Comparison	**Parameter**	**Mean Difference**	**p-value**
Group A vs Group C	VD 1 mm center	-1.6	<0.01
Group A vs Group C	PD inner ring	-2.1	<0.01
Group B vs Group D	VD 3 mm full	-1.1	0.02
Group B vs Group D	FAZ area	0.03	0.01
Group A vs Group B	GC-IPL	-2	0.04
Group A vs Group B	RNFL	-3	0.03

Discussion

This study's findings support that chronic hypertension has a relevant effect on both the vasculature and structural integrity of the retina in the undergraduate medical student population, which corresponds to previous research indicating the involvement of microvascular in the systemic hypertension. We found that the lowest values of vessel density (VD) and perfusion density (PD) were found in patients with chronic hypertension (Group A), in contrast to younger healthy controls (Group D), with VD center of 1 mm being 18.5 ± 1.2 mm/mm 2 and PD center of 1 mm being 42.3 ± 2.5 in Group A compared to 20.3 ± 1.0 mm/mm 2 of the VD and 44.8 ± 2.1 of the PD in the center of 1 mm of the 1 mm central macula in Group D. These age-dependent alterations in the microvascular metrics are consistent with the findings of Muraoka et al. (2013) [9] who reported systemic blood pressure-dependent age-related losses of retinal vessel diameter and retinal perfusion and concluded that chronic exposure of uncontrolled elevations in systemic blood pressure cause microvascular rarefaction and structural remodelling of the retinal capillaries. Additionally, Wong et al. (2002)

[10] found that retinal arteriolar constriction associated with increased cardiovascular risk in hypertensive patients, and further reported that retinal microcirculation is a candidate surrogate endpoint of systematic vascular state.

We have also observed that the foveal avascular zone (FAZ) was greatly expanded among those with chronic hypertension (0.32 ± 0.04 mm 2 in Group A), and it reduced gradually between relieved hypertension (Group B) and controls. This tendency confirms the assumption that chronic hypertension causes microvascular dropout, which can be one of the factors contributing to compensatory retinal thinning. The current findings are similar to those of Lee et al. (2018) [11] who noted the atrophy of FAZ area and simultaneous atrophy of central macular thickness (CMT) and ganglion cell-inner plexiform layer (GC-IPL) in patients with severe hypertensive retinopathy, which supports the idea that the process of microvascular compromise is highly interconnected with structural retinal alterations. In our experiment Group B (religed hypertension) showed improvement (partially), which means that at least partially, microvascular changes are reversible on effective blood pressure management. This is in contrast to hypertensive eyes that have been chronic, which have shown some sustained deficits, hence the importance of ensuring that blood pressure is checked early and through constant monitoring.

OCT of the structure showed thinning of CMT, GC-IPL and retinal nerve fiber layer (RNFL) in chronic hypertensive patients, with mean differences of -2 μm and -3 μm of GC-IPL and RNFL respectively compared to relieved hypertensive group. The results are consistent with those published by Lee et al. (2018), who have found that inner retinal layers in hypertensive patients were significantly thinning, which is why the loss of neurons might be observed before the visual impairment is detected. The correlation of OCTA parameters with OCT measures shows further that the relationship between microvascular and structural changes is significant, and the correlation coefficient of OCTA parameters with OCT measures in the relieved hypertensive group (r = 0.5290.716) is significantly larger than in chronic hypertensives (r = 0.347398).

Comparisons on the inter-group basis in our research indicated statistically significant differences, with Group A having low VD in the 1 mm central macula (mean difference -1.6 mm/mm 2, $p < 0.01$) and low PD in the inner ring (mean difference -2.1, $p < 0.01$) compared with age-matched controls (Group C). These results are consistent with Rizzon et al. (2012) who highlighted that hypertensive microvascular remodelling in the retina is related to changes in the small arteries in the system, which support the idea that the retina is a window into the health of the systemic vasculature. Interestingly, at hypertension relief, Group B participants had lower VD in the 3 mm full macula and an enlarged FAZ than younger controls, consistent with reports by Thom et al. (2009) that antihypertensive treatment can reverse but not normalize retinal microvascular changes.

Methodological considerations and limitations to OCTA imaging are also noted in our study. Although the eye-tracking and small 3 x 3 mm macular scans are used, motion artifacts have resulted in the exclusion of 16 eyes, which is in line with the literature mentioning that OCTA images are prone to pupil vignetting, defocus, and segmentation errors (Spaide et al., 2015; Say et al., 2017). Nonetheless, OCTA parameter intraclass correlation coefficients were above 0.8, which implies that it has high repeatability. In future research, the sample sizes need to be larger and prospective longitudinal designs need to be implemented to determine the relationship between the retinal microvascular rarefaction and structural thinning over time, especially of young adults with hypertension since the onset of hypertension.

Our research confirms and enhances prior evidence, indicating that chronic hypertension is associated with decreased macular perfusion, increased FAZ, and thinning of retinal neuronal layers, and that effective blood pressure control can partially reverse these changes. The relationships between both OCTA and OCT measurements add to the functional-structural relationship in retinal microcirculation and suggest the potential of OCTA as a noninvasive marker of early hypertensive retinal involvement and systemic microvascular risk.

Conclusion

This study demonstrates that hypertension exerts a significant impact on both the vascular and structural integrity of the retina. Chronic hypertensive individuals exhibited reduced vessel density and perfusion, enlarged foveal avascular zones, and thinning of the ganglion cell-inner plexiform layer and retinal nerve fiber layer, indicating microvascular rarefaction and neuronal compromise. Participants with relieved hypertension showed partial recovery, suggesting that early detection and effective blood pressure management can mitigate, but not entirely reverse, retinal alterations. The observed correlations between OCTA and OCT parameters emphasize the close relationship between microvascular and structural retinal changes. Overall, retinal imaging serves as a valuable, non-invasive tool for detecting hypertensive end-organ damage, providing insights into systemic vascular health and informing strategies for timely intervention to prevent vision-threatening complications.

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