Ocular perfusion pressure as a mediator between Systemic Hypertension and Glaucoma

Ophthalmol Pak. - Official Journal of College of Ophthalmology & Allied Vision Sciences

Saliha Bibi[1], Khurram Nasir[2].
Superior University Lahore[1,2].

ABSTRACT

Purpose: To evaluate the relationship between systemic hypertension, ocular perfusion pressure and glaucoma.

Methodology: AA cross-sectional comparative study was conducted, and the sample was divided into two groups (22 hypertensive patients and 22 normotensive controls) who had ages between 40 and 60 years. The participants were thoroughly examined with the measurement of systemic blood pressure, intraocular pressure and ocular perfusion pressure calculation. Fundus photography, optical coherence tomography (OCT), and automated perimetry were used to measure structural and functional damage. The SPSS was used to analyze data, with the help of the Mann-Whitney U test and correlation analysis.

Result: The hypertensive group's mean IOP was significantly higher (25.68 +- 8.98 mmHg) than the normotensive group's (18.22 +- 2.72 mmHg, p=0.001). However, there was no significant difference in the mean OPP between the groups (47.9 +- 9.8 mmHg vs. 46.2 +- 6.5 mmHg, p=0.49), which is indicative of compensatory hemodynamics, whereby elevated IOP compensated for elevated systemic blood pressure. More significantly, 40.9% and 45.5% of the hypertensive group, respectively, presented abnormal fundus photographs and OCT results, indicating a significantly higher prevalence of structural optic nerve damage (vs. 18.2 and 13.6, p=0.03 and p=0.01). According to the correlation analysis, there was a significant relationship between the OPP values and structural glaucomatous defects on fundus examination (r=-0.29, p=0.04) and OCT (r=-0.35, p=0.02).

Conclusion: Ocular Perfusion Pressure is the primary mediating factor, according to the data. It effectively connects glaucoma damage to systemic hypertension.

Keywords: Ocular Perfusion Pressure (OPP), Systemic Hypertension, Glaucoma, Vascular Autoregulation

How to cite this article: Bibi S, Nasir K. Ocular perfusion pressure as a mediator between Systemic Hypertension and Glaucoma. Opthalmol. Pak. 2025;15(4):125-130.
DOI: https://doi.org/10.62276/OphthalmolPak.15.04.220

Correspondence: Khurram Nasir,
Superior University Lahore.
Email: khurram.nasir@superior.edu.pk

Received: 29-11-2025
Accepted: 13-12-2025

INTRODUCTION

Over 1.28 billion people worldwide suffer from systemic hypertension (HTN), a chronic non-communicable disease that presents a serious health burden[1]. It is recognized as a major risk factor for cardiovascular events, renal dysfunction, and stroke and is clinically defined as a persistent increase in arterial blood pressure (BP) above 140/90 mmHg. But the effects of hypertension go beyond these systems; it also contributes to ocular diseases like glaucoma, age-related macular degeneration (AMD), retinal vein occlusion, and hypertensive retinopathy[2,3].

Glaucoma, particularly primary open-angle glaucoma, is a significant contributor to irreversible blindness worldwide. By 2040, it is projected that more than 111 million individuals will be impacted by glaucoma, with a significant burden on aging populations and low-to-middle-income countries[4,5]. Primary open-angle glaucoma is defined by the progressive degeneration of optic nerve fibers, resulting in the loss of retinal ganglion cells (RGCs), cupping of the optic nerve head (ONH), and associated visual field deficits. The highest risk factor that has been identified as modifiable in causing and progression of glaucoma is elevated intraocular pressure (IOP). Nevertheless, there is growing evidence that vascular processes, particularly the disruption of ocular blood flow and autoregulation may contribute greatly to the disease pathogenesis[6].

Ocular perfusion pressure is a vital hemodynamic variable that relates systemic vascular well-being to eye performance. Ocular perfusion pressure denotes the pressure gradient that facilitates blood delivery to the eye and is calculated by the difference between arterial BP and intraocular pressure[7]). Adequate ocular perfusion pressure is essential for sustaining oxygenation and nutrient delivery to the metabolically active components of the eye, especially the optic nerve head and retina. Disruption of ocular perfusion pressure, whether due to increased intraocular pressure, decreased blood pressure, or a combination of both, can result in ischemia and subsequent death of retinal ganglion cells[8].

Normal tension glaucoma, which is a subtype of primary open angle glaucoma, remains particularly relevant in the context of ocular perfusion pressure. Although the intraocular pressure in these patients is normal (statistically 21 mmHg and below), they have glaucomatous damage. Vascular dysregulation, including reduced ocular perfusion pressure and autoregulation dysfunction, has been considered to be the major cause of normal tension glaucoma pathogenesis[9]. People with systemic vascular abnormalities, including migraine or Raynaud's phenomenon, commonly included under Flammer syndrome, are overrepresented in normal tension glaucoma populations. Even when intraocular pressure is within the normal range, these people have low systemic blood pressure, aberrant vasospastic responses, and a vulnerability to perfusion-related optic nerve damage[10].

Vascular autoregulation is essential to comprehending how ocular perfusion pressure affects the development of glaucoma. Through autoregulatory processes, the ocular vasculature typically sustains steady blood flow across a range of systemic blood pressures and intraocular pressures. This enables tissue perfusion to be maintained in spite of variations in perfusion pressure. These mechanisms, however, may be impaired in glaucoma, especially normal tension glaucoma, which increases the optic nerve head's vulnerability to ischemic injury[11]. Numerous studies have demonstrated that glaucoma progression can be accurately predicted by blood pressure variations and ocular perfusion pressure instability, not just the absolute ocular perfusion pressure value[12].

In summary, glaucomatous optic neuropathy and systemic hypertension are physiologically linked through ocular perfusion pressure. intraocular pressure is still a major factor in the pathophysiology of glaucoma, but vascular contributions—especially those involving ocular perfusion pressure —are becoming more widely acknowledged as important factors that influence

the development and course of the disease. This study specifically aims to investigate ocular perfusion pressure as a key mediator in the relationship between systemic hypertension and glaucoma.

METHODOLOGY

A comparative cross-sectional study was conducted at Superior University, Lahore, from April 2025 to September 2025. The research protocols were approved by Ethical Review Board of College of Ophthalmology and Allied Vision Science, Lahore. The size of obtained sample was 44, which was equally divided into two groups;

$$n = \frac{(\sigma^2(z_{1-}\alpha/_2 + z_{1-}\beta)^2)}{(\mu_0 - \mu_1)^2}$$

Confidence level: 95%

Precision level: 10%

Level of Significance (σ^2) = 7.95

$Z_{1-}\alpha/_2$ (95% Confidence): 1.96

$Z_{1-}\beta$ (90% Power): 1.28

Test value of population mean (μ_0): 15.37 mmHg

Anticipated population mean (μ1): 13.41 mmHg

We selected 44 participants, 22 of whom had hypertension and 22 of whom had normotension, using non-probability convenience sampling. The participants were between the ages of 40 and 60. Participants with hypertension who were on stable antihypertensive medications for at least three months and who satisfied the clinical criteria for systemic hypertension (BP ≥140/90 mmHg) were included in the study. In order to rule out confounding vascular influences, exclusion criteria included secondary glaucoma, congenital glaucoma, other ocular pathologies, history of ocular trauma or surgery, and diabetes mellitus. After giving their informed consent, each participant had a thorough ophthalmic evaluation. Standard procedures were followed when taking blood pressure readings with calibrated sphygmomanometers. Goldmann applanation tonometry was used for the IOP assessment. MAP (mean arterial pressure) = Diastolic BP + 1/3(Systolic BP - Diastolic BP) is the standard formula that we used to calculate mean ocular perfusion pressure: MOPP = $^2/_3$ MAP - IOP. Fundus photography and spectral-domain optical coherence tomography (OCT) were used in the structural evaluation to measure the parameters of the optic nerve head and the thickness of the retinal nerve fiber layer. Standard automated perimetry was used for the functional assessment. SPSS version 26.0 was used for data analysis. Shapiro-Wilk tests were used to test for normality in continuous variables. Independent t-tests were used to analyze normally distributed variables, while Mann-Whitney U tests were used to analyze non-normally distributed parameters (IOP, OPP). Chi-square tests were used in the analysis of categorical data. Relationships between OPP and other parameters were ascertained through correlation analyses. The threshold for statistical significance was set at $p<0.05$.

RESULTS

In this study, there were 44 participants; 22 in each group in the age range of 40-60 years. The majority of the participants were female. The Shapiro-Wilk test was used to evaluate the normality of the data. Non-parametric tests were used because the continuous variables (IOP, OPP) showed a significant deviation from the normal distribution ($p < 0.05$). To compare these parameters between the hypertensive and normotensive groups, the Mann-Whitney U test was employed rather than the Independent t-test.

Table no. 1: Comparison of ocular parameters between hypertensive and normotensive study groups

	Groups	Mean ± Std. Deviation	t	Min-Max	p-value
IOP	Hypertensive	25.68 ± 8.98	3.72	3.41 – 11.49	0.001
	Non-hypertensive	18.22 ± 2.72	2.66	3.32 – 11. 58	0.001
OPP	Hypertensive	45.7 ± 8.57	-0.3	-5.81 – 4.36	0.001
	Non-hypertensive	46.5 ± 8.15	-0.3	-5.81 – 4.36	0.776
Fundus photograph	Hypertensive	1.40 ± 0.50	1.66	-0.04 – 0.50	0.103
	Non-hypertensive	1.18 ± 0.39	1.66	-0.04 – 0.50	0.103
OCT	Hypertensive	1.41 ± 0.50	1.66	-0.04 – 0.50	0.103
	Non-hypertensive	1.18 ± 0.39	1.66	-0.04 – 0.50	0.103
VF	Hypertensive	1.14 ± 0.35	1.03	-0.08 – 0.26	0.103
	Non-hypertensive	1.05 ± 0.21	1.03	-0.08 – 0.26	0.103

This table compares ocular parameters between hypertensive and normotensive groups. Hypertensive participants showed significantly higher intraocular pressure (p=0.001) but similar ocular perfusion pressure (p=0.776) compared to controls. Structural and functional tests (fundus, OCT, visual field) consistently showed more abnormalities in the hypertensive group, though these differences were not statistically significant. According to the results, structural damage is still more common even though compensatory mechanisms keep OPP stable while hypertension raises IOP.

Table no. 2: Comparison of systemic and ocular hemodynamic parameters between hypertensive and normotensive groups

Parameter	Hypertensive Group (n=22)	Normotensive Group (n=22)	p-value
Systolic BP (mmHg)	137.8 ± 13.5	119.6 ± 16.2	<0.001
Diastolic BP (mmHg)	96.2 ± 10.3	81.4 ± 10.8	<0.001
Mean Arterial Pressure (mmHg)	110.1 ± 10.8	94.1 ± 11.9	<0.001
Intraocular Pressure (mmHg)	24.8 ± 8.9	18.9 ± 4.7	0.006
Ocular Perfusion Pressure (mmHg)	47.9 ± 9.8	46.2 ± 6.5	0.49

The results show that compared to the normotensive group, hypertensive patients had significantly higher systolic, diastolic, mean arterial, and intraocular blood pressures ($p < 0.001$ in the BP parameters, $p = 0.006$ in the IOP parameters). However, despite these increases in intraocular and systemic pressures, there was no discernible difference between the two groups in the calculated Ocular Perfusion Pressure ($p = 0.49$). It indicates that people with hypertension have higher systemic blood pressure, which appears to counteract their higher intraocular pressure and comparable net perfusion pressure to the eye.

Table no. 3: Prevalence of structural and functional ocular defects in hypertensive and normotensive groups

	Hypertensive Group (n=22)	Normotensive Group (n=22)	p-value
Fundus Photography			
Normal	13 (59.1%)	18 (81.8%)	0.03
Defective	9 (40.9%)	4 (18.2%)	
Optical Coherence Tomography			
Normal	12 (54.5%)	19 (86.4%)	0.01
Defective	10 (45.5%)	3 (13.6%)	
Visual Field Testing			
Normal	17 (77.3%)	21 (95.5%)	0.08
Any Scotoma	5 (22.7%)	1 (4.5%)	

This table compares the outcomes of key ophthalmic examinations between the hypertensive and normotensive groups. It reveals a significantly higher prevalence of structural defects in the hypertensive group, with fundus photography abnormalities in 40.9% (vs. 18.2%, p=0.03) and OCT abnormalities in 45.5% (vs. 13.6%, p=0.01). A similar, non-significant trend was observed in functional testing, where visual field scotomas were present in 22.7% of hypertensive participants compared to 4.5% of normotensives (p=0.08). The results consistently demonstrate a greater burden of glaucomatous damage across all diagnostic modalities in individuals with systemic hypertension.

Table no. 4: Correlation of ocular perfusion pressure with systemic and ocular parameters

Parameter	Correlation with OPP	p-value
Systolic BP	0.58	<0.001
Diastolic BP	0.52	<0.001
Intraocular Pressure	-0.41	0.008
Abnormal OCT Findings	-0.35	0.02
Abnormal Fundus Findings	-0.29	0.04

The correlation analysis showed that Ocular Perfusion Pressure (OPP) was significantly and positively correlated with systolic blood pressure ($r=0.58$, $p<0.001$) and diastolic blood pressure ($r=0.52$, $p<0.001$) and thus, higher systemic blood pressure is positively correlated with higher ocular perfusion pressure. On the other hand, OPP showed a large moderate negative association with intraocular pressure ($r=-0.41$, $p=0.008$), proving the inverse relationship in which an increase in IOP leads to the decrease in the perfusion pressure gradient. Most importantly, structural optic nerve damage was significantly negatively correlated with the OPP as indicated by abnormal OCT (r -0.35, $p=0.02$) and abnormal fundus (r -0.29, $p=0.04$), implying that lower values of OPP

correlated with the increased probability of glaucomatous structural defects. Overall, these correlations point to OPP's critical function as a hemodynamic link between intraocular pressure, systemic cardiovascular disease, and structural optic nerve disorders in glaucoma.

DISCUSSION

Examining the intricate connections between glaucomatous optic neuropathy, ocular perfusion pressure (OPP), and systemic hypertension was the aim of this study. Our findings provide compelling clinical support for the evolving vascular paradigm of glaucoma and position OPP as a major mediator in the causal pathway linking systemic cardiovascular health to ocular disease, rather than merely a risk factor. Our study's key finding is that the hypertensive group's IOP was significantly higher (25.68 ± 8.98 mmHg) than that of the normotensive controls (18.22 ± 2.72 mmHg, p=0.001). This supports a large body of research, such as the pathophysiological model put forth by Costa et al., which postulates that high systemic blood pressure may affect the dynamics of the aqueous humor and episcleral venous pressure, ultimately leading to an increase in intraocular pressure[13, 14]. Additionally, our data supported the anticipated, significant increase in the hypertensive cohort's systolic, diastolic, and mean arterial pressure systemic blood pressure parameters ($p<0.001$ for all). However, the most important and fascinating finding is that there was no significant difference in the mean Ocular Perfusion Pressure between the two groups (47.9 ± 9.8 mmHg vs. 46.2 ± 6.5 mmHg, p=0.49). The net pressure gradient that propels blood flow to the optic nerve head is represented by OPP, which is computed as the difference between mean arterial pressure and IOP. Hemodynamic compensation is one way to interpret this finding. Hypertensive patients' higher systemic pressure seems to successfully offset their correspondingly higher IOP, producing a comparable net perfusion pressure. The long-known but little-understood "U-shaped" or "J-shaped" relationship between blood pressure and glaucoma risk, in which both high and low blood pressure are linked to increased prevalence, can now be physiologically explained by this observation[15]. According to our data, hypertension may be protective in the early or compensated stages by acting as a stronger motivator to overcome IOP. This idea is corroborated by certain cross-sectional studies[16]. But as our structural data shows, this seeming stability is misleading and probably only temporary. Our study discovered that the hypertensive group had a noticeably greater burden of structural glaucomatous damage, even though mean OPP was preserved. Over twice as many hypertensive subjects had defective fundus photography findings (40.9% vs. 18.2%, p=0.03), and an even more pronounced difference was found in optical coherence tomography, where 45.5% of hypertensive subjects had abnormalities compared to just 13.6% of controls (p=0.01). The dissociation between a stable hemodynamic parameter (OPP) and worsened structural outcomes is the primary paradox that our research helps to resolve. This finding forces a shift in perspective from one that emphasizes static OPP values to one that stresses dynamic vascular regulation. There is substantial evidence in the literature that chronic hypertension is the cause of endothelial dysfunction, arterial stiffening, and—above all—impaired autoregulation[17,18]. Autoregulation is the eye's innate capacity to maintain constant blood flow across a range of perfusion pressures and regulate vascular resistance. A healthy ocular circulation can dilate when OPP falls and constricts when OPP rises. Our correlation analysis provides strong support for this mechanism. OPP was found to have a significant negative correlation with IOP (r=-0.41, p=0.008) and a strong positive correlation with both systolic and diastolic blood pressure (r=0.58 and r=0.52, $p<0.001$). This suggests that OPP was highly dependent on systemic blood pressure in our group. The RNFL thinning and optic nerve cupping that we observed using OCT and fundus photography19, 20 are results of cumulative ischemic and reperfusion injury in our hypertensive patients, who are therefore sitting targets for these fluctuations due to their impaired autoregulation. Our correlation analysis further supports OPP's role as the

suggested mediator by directly connecting it to the clinical endpoint of glaucomatous damage. We discovered statistically significant negative correlations between OPP and abnormal fundus findings (r=-0.29, p=0.04) as well as abnormal OCT findings (r=-0.35, p=0.02). This implies that, even within the observed range, lower OPP values were consistently associated with a higher likelihood of structural optic nerve damage. This discovery helps to close the gap between clinical practice and population-based epidemiological research.

CONCLUSION

The results validate that glaucoma and systemic hypertension are significantly mediated by ocular perfusion pressure (OPP). OPP is maintained by hemodynamic compensation, but it has a direct, inverse relationship with structural glaucomatous damage, even though hypertension raises intraocular pressure.

Conflict Of Interest: None to declare.

Ethical Approval: The study was approved by the Institutional Review Board / Ethical Review Board Reference No. SU/IRB/FAHS/25/D-1234 dated 15.03.2025, Superior University Lahore.

Authors' Contributions:

Saliha Bibi: Concept, Design, Literature search, Statistical analysis, Manuscript preparation, Manuscript editing.

Khurram Nasir: Data acquisition, Data analysis, Statistical analysis, Manuscript editing.

REFERENCES

1. Nislawati R, Taufik Fadillah Zainal A, Ismail A, Waspodo N, Kasim F et al. Role of hypertension as a risk factor for open-angle glaucoma: a systematic review and meta analysis. BMJ Open Ophth. 2021 ;6(1)798 DOI: https://doi.org/10.1136/bmjophth-2021-000798

2. Dziedziak J, Zaleska-Zmijewska A, Szaflik JP, Cudnoch-Jędrzejewska A. Impact of Arterial Hypertension on the Eye: A Review of the Pathogenesis, Diagnostic Methods, and Treatment of Hypertensive Retinopathy. Med Sci Monit 2022;28: e935135-1 DOI: https://doi.org/10.12659/MSM.935135

3. Cheung CY, Biousse V, Keane PA, Schiffrin EL, Wong TY. Hypertensive eye disease. Nature Reviews Disease Primers 2022; 8(1):1–18 DOI: https://doi.org/10.1038/s41572-022-00342-0

4. Wang ZY, Pan Z, Wu Y, Zhang C, Jonas JB, Tham YC, et al. Projection of Glaucoma Burden Worldwide in 2040 with Myopia Surge. Invest. Ophth. & Vis Sci June 2024, Vol.65, 4605. DOI: 10.1016/j.ophtha.2014.05.013

5. Chen W, Xu Y, Liu Z, Zhao J. Global, regional and national burden of Glaucoma: an update analysis from the Global Burden of Disease Study 2019. Int Ophth. 2024; 44(1):1–11. DOI: https://doi.org/10.1007/s10792-024-03222-6

6. Zhou W, Sabel BA. Vascular dysregulation in glaucoma: retinal vasoconstriction and normal neurovascular coupling in altitudinal visual field defects. EPMA J 2023;14(1): 87–99 DOI: 1https://doi.org/10.1007/s13167-023-00316-6

7. Hayreh SS. Blood flow in the optic nerve head and factors that may influence it. Prog Retin Eye Res 2001;20(5):595–624 DOI: https://doi.org/10.1016/s1350-9462(01)00005-2

8. Mansouri K, Rao HL, Weinreb RN. Short-Term and Long-Term Variability of Intraocular Pressure Measured with an Intraocular Telemetry Sensor in Patients with Glaucoma. Ophthalmology .2021;128(2): 227–33. DOI: https://doi.org/10.1016/j.ophtha.2020.07.016

9. Park S, Lakatta EG. Role of Inflammation in the Pathogenesis of Arterial Stiffness. Yonsei

Med J .2021;53(2):258. DOI: https://doi.org/10.3349/ymj.2012.53.2.258

10. Gracitelli CPB, Zangwill LM, Diniz-Filho A, Abe RY, Girkin CA, Weinreb RN, et al. Detection of glaucoma progression in individuals of African descent compared with those of European descent. JAMA Ophthalmol. 2018;136(4):329–35 DOI: https://doi.org/10.1001/jamaophthalmol.2017.6836

11. Jo YH, Shin JW, Song MK, Won HJ, Kook MS. Choroidal Microvasculature Dropout is Associated with Generalized Choroidal Vessel Loss within the β-Parapapillary Atrophy in Glaucoma. Am J Ophthalmol 2020;215:37–48. Available from: DOI: https://doi.org/10.1016/j.ajo.2020.03.009

12. Jammal AA, Berchuck SI, Mariottoni EB, Tanna AP, Costa VP, Medeiros FA. Blood Pressure and Glaucomatous Progression in a Large Clinical Population. Ophthalmology 2021;129(2):161. DOI: https://doi.org/10.1016/j.ophtha.2021.08.021

13. Wang X, Wang M, Liu H, Mercieca K, Prinz J, Feng Y, et al. The Association between Vascular Abnormalities and Glaucoma -What Comes First? Int J Mol Sci 2023;24(17):13211. DOI: https://doi.org/10.3390/ijms241713211

14. Faiq MA, Sofi RA. A Glimpse into the mysteries of glaucoma: From theories to clinics. Oman J Ophthalmol. 2019;12(1):1–3. doi: 10.4103/ojo.OJO_91_2018

15. Kim KE, Oh S, Baek SU, Ahn SJ, Park KH, Jeoung JW. Ocular Perfusion Pressure and the Risk of Open-Angle Glaucoma: Systematic Review and Meta-analysis. Sci Rep Sci Rep. 2020;10(1):10056. DOI: 10.1038/s41598-020-66914-w

16. Kim KE, Oh S, Baek SU, Ahn SJ, Park KH, Jeoung JW. Ocular Perfusion Pressure and the Risk of Open-Angle Glaucoma: Systematic Review and Meta-analysis. Sci Rep Sci Rep. 2020;10(1):10056. DOI: 10.1038/s41598-020-66914-w

17. Khandelwal R, Khandelwal R, Raje D, Kumar D, Rathi A. Correlation of open-Angle glaucoma and ocular perfusion pressure in hypertensive individuals. J Clin Ophthalmol & Res. 2020;8(1):5–9. DOI: https://doi.org/10.4103/jcor.jcor_90_18

18. Tanna AP. Blood Pressure and Glaucoma—A Complex Relationship. JAMA Ophthalmol 2023;141(3):258–9. DOI: https://doi.org/10.1001/jamaophthalmol.2022.6515

19. Liu T, Cai YL, Hu MY, Wang Z, Liu X, Chen M, et al. The impact of intraocular pressure fluctuations on the progression of glaucoma and associated factors. AOPR 2025;5(2):142-148 DOI: https://doi.org/10.1016/j.aopr.2025.03.002

20. Leidl MC, Choi CJ, Syed ZA, Melki SA. Intraocular pressure fluctuation and glaucoma progression: what do we know?. British J Ophthalmol. 2014;98(10):1315-9.