Correlation of open-angle glaucoma and ocular perfusion pressure in hypertensive individuals

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Background: Systemic hypertension has been recognized as a potential risk factor for primary open-angle glaucoma (POAG). Purpose: The purpose of this study is to study the correlation of systemic blood pressure, intraocular pressure (IOP), and ocular perfusion pressure (OPP) for the development of glaucoma in hypertensive individuals. Methods: After Institutional Ethics Committee approval, a hospital-based case-control study was conducted in a tertiary care hospital. The study group comprised of patients with systemic hypertension, and the control group had the age- and sex-matched normotensives. POAG was diagnosed if glaucomatous cupping and characteristics visual field defects were present with open angles on gonioscopy. OPP was compared between POAG and non-POAG groups. Results: In this study of 103 hypertensive and 100 normotensive patients, the mean IOP was higher among hypertensives. There were 9 (8.74%) cases of POAG in hypertensive group and 2 (2%) in the normotensive group. The mean IOP in hypertensive group was 16.5 ± 4.5 mmHg, and that of normotensive group was 13.14 ± 3.19 mmHg. The mean OPP in hypertensive patients with glaucoma was 49.38 ± 2.6 mmHg, which was significantly lower than that of patients without glaucoma, i.e., 60.16 ± 5.42 mmHg, as indicated by P < 0.001. Conclusion: This study reveals that hypertensive patients taking anti-HT treatment with POAG have lower mean OPP as compared to those without POAG. The higher OPP could be protective against glaucomatous condition; however, interdisciplinary management of open-angle glaucoma and hypertension is the need for a better quality of life of such patients.

Key words: Intraocular pressure, ocular perfusion pressure, primary open-angle glaucoma, systemic hypertension.

Glaucost is a group of ocular disorders characterized by optic neuropathy and visual field loss. This may or may not be accompanied by a rise in intraocular pressure (IOP). It is a chronic progressive disease and eventually leads to irreversible form of blindness. In India, glaucoma is estimated to affect over 11 million people[7] and is the third most common cause of blindness after cataract and corneal blindness.[8]

Vascular risk factors such as systemic hypertension, atherosclerosis, and vasospasm have been recognized as potential factors that are capable of increasing the risk of primary open-angle glaucoma (POAG) and normal tension glaucoma (NTG).[9,10] It has been hypothesized that low blood pressure (BP) relative to IOP leads to low ocular perfusion pressure (OPP) of the optic nerve leading to glaucomatous disc changes and visual field loss.[11,12]

Chronically elevated BP leads to arteriosclerotic changes and changes in the size of the precapillary arterioles which gives rise to increased resistance to blood flow and hence reduced perfusion.[13] In the Blue Mountain Eye Study and the Egna-Neumarkt study, the association has been found between POAG and systemic hypertension.[7,8] In contrast, studies performed by Deb et al. and Vijaya et al. have reported no significant association between the two.[9,10]

Recent literature suggests that the measurement of OPP is a highly relevant parameter in open-angle glaucoma patients.[14] Fluctuations in the OPP is a known contributing factor in the development of glaucomatous disc changes in the subgroup of POAG, as known as NTG.[15]

It has also been observed that individuals on antihypertensive medications were 2–3 times more likely to be affected by glaucoma. This may be attributed to the bedtime dosage of antihypertensive drugs which cause a drop in nocturnal BP, eventually leading to a reduction in OPP[9]

A study performed by Pache and Flammer reported a nocturnal dip in BP as an important risk factor for POAG.[14] The Thessaloniki eye study noted that lowering of BP from...
antihypertensive treatment was associated with glaucomatous changes.\(^{[15]}\)

With the above context, the present study was designed to analyze the relationship between POAG and OPP in hypertensive patients as compared to normotensive patients.

**Methods**

After Institutional Ethics Committee approval following the tenets of the Declaration of Helsinki, a hospital-based case–control study was carried out in a tertiary healthcare center attached to an academic institute. The study group included either self-reported or newly diagnosed cases of systemic hypertension \((n = 103)\) attending once a week medicine outpatient department (OPD) of a senior physician (RM) during 2 months. Informed consent was taken from all the individuals in their vernacular language (Hindi/Marathi). The demographic details of all individuals were recorded in the Case Record form. Individuals more than 40 years of age, either sex were included in the study. Systemic hypertension was defined as the systolic BP (SBP) \(\geq 140\) mmHg and/or Diastolic BP (DBP) \(\geq 90\) mmHg. Detailed history regarding the duration of hypertension, family history, and antihypertensive medications was recorded. Patients with diabetes mellitus and thyroid disorders were excluded from the study. Patients with hypertension due to secondary causes (endocrine, kidney, or steroid use) and poor medical condition (illness), trauma, comatose, and unwilling to participate were also excluded from the study. The control group comprised of age- and sex-matched normotensive participants \((n = 100)\) attending eye OPD during the same 2 months of the study.

Single measurement of BP was taken for all the individuals in the right upper arm in the sitting position using a mercury sphygmomanometer (as per the American Heart Association BP measurement recommendation).

Comprehensive glaucoma evaluation was performed on individuals of both the groups by the guide (Senior Ophthalmologist). This included Slit Lamp examination, IOP measurement by Goldmann Applanation tonometer, Zeiss 4 mirror gonioscopy, optic disc evaluation by 90D Volk Lens, and Visual Field charting by 24-2 Humphrey Field Analyzer.

Automated perimetry (Thresholding Algorithm 24-2; Humphrey Field Analyzer; Carl Zeiss AG) were performed on all the patients and repeated if the test reliability was not satisfactory (fixation loss >20%, false positive >33%, or false negative >33%) or there was a glaucomatous field defect.

POAG was diagnosed if glaucomatous cupping and characteristics field defects were present along with thinning of retinal nerve fiber layer in the presence of open angles on 4-mirror gonioscopy. The patients were categorized on the basis of the International Society of Geographical and Epidemiological Ophthalmology Classification scheme.

The diagnosis was made according to three levels of evidence.

**Category 1 diagnosis** (structural and functional evidence) – Eyes with a cup-disc ratio (CDR) or CDR asymmetry \(\geq 97.5^{th}\) percentile for the normal population, or a neuroretinal rim width reduced to \(\leq 0.1\) CDR (between 11 and 1 o’clock or 5 and 7 o’clock) that also showed a definite visual field defect consistent with glaucoma.

**Category 2 diagnosis** (advanced structural damage with unproved field loss) – If the individual could not satisfactorily complete visual field testing but had a CDR or CDR asymmetry \(\geq 99.5^{th}\) percentile for the normal population, glaucoma was diagnosed solely on the structural evidence.

**Category 3 diagnosis** (Optic disc not visible, VF test not possible) – If it was not possible to examine the optic disc, glaucoma is diagnosed if: (A) the visual acuity <3/60 and the IOP >99.5\(^{th}\) percentile, or (B) the visual acuity <3/60 and the eye showed evidence of glaucoma filtering surgery, or medical records were available confirming glaucomatous visual morbidity.

Those with normal IOP with the typical disc and field changes were classified as NTG while those who presented with raised IOP with glaucomatous disc and field changes were termed as POAG. Ocular hypertension was defined as IOP more than 21 mmHg with normal disc and fields. The findings were recorded using standardized glaucoma assessment tool (case record form).

OPP was calculated by the standard formula as follows:

\[
\text{OPP} = \frac{2}{3} \times (\text{MAP-IOP})
\]

Where, mean arterial pressure (MAP) = DBP + 1/3(SBP-DBP)

The baseline characteristics of patients were summarized according to the scale of measurement in both hypertensive and normotensive groups. The continuous parameters were evaluated for significance of the difference between two groups using t-test of independent samples, while parameters on nominal scale were evaluated using Pearson’s Chi-square test. The comparison of mean IOP and OPP across hypertensive (on anti-HT drugs and not on anti-HT drugs) and normotensive patients was performed using one-way analysis of variance. Paired comparison between groups was carried out using Tukey’s post hoc test. Further, the comparison of OPP between hypertensive and normotensive patients with and without POAG was performed using t-test for independent samples. The statistical significance was tested at 5% level, and all the analyses were performed using SPSS version 20 (IBM Corp. Armonk, USA).
Results

A total of 203 individuals participated in this study. There were 103 patients in the hypertensive group, and equivalently age- and gender-matched 100 individuals in the control group. The baseline characteristics in the two study groups are shown in Table 1. The mean systolic, DBP and MAP were significantly higher in hypertensive group as compared to normotensive group. There were 9 (8.74%) cases of POAG in hypertensive group and 2 (2%) cases in the normotensive group. The mean IOP as well as OPP in hypertensive group was statistically higher than normotensive group, as shown in Table 2. Of 103 hypertensive patients, 76 were taking antihypertensive drugs, while 27 were not on any medication. Table 3 shows that mean IOP across hypertensive with or without medication and normotensive individuals were significantly different as indicated by \( P < 0.001 \). The mean IOP of hypertensive patients on medication (16.63 ± 4.75 mmHg) was insignificantly different than those without medication (16.15 ± 3.79 mmHg), while the mean IOP of normotensive (13.14 ± 3.19 mmHg) was significantly lower than hypertensive groups, as obtained through pairwise post hoc analysis. The mean OPP across groups also differed significantly \( (P < 0.001) \). The post hoc analysis revealed that the mean OPP for hypertensive patients on medication (56.44 ± 3.80 mmHg) differed insignificantly from that of normotensive group (55.41 ± 3.50 mmHg); however, these means were significantly lower than that of hypertensive patients without medication (67.05 ± 4.04 mmHg).

The analysis of mean OPP was also performed considering the POAG status of individuals, as shown in Table 4. There were 8 individuals with POAG and on anti-HT treatment, while only 1 with POAG but without anti-HT treatment. Hence, comparison of OPP was performed between hypertensive patients on treatment and normotensive group. The mean OPP between hypertensive patients on anti HT treatment (48.67 ± 1.67 mmHg) was insignificantly different than normotensive group (46.23 ± 0.95); however, in the non-POAG group, the mean for hypertensive patients (60.16 ± 5.42 mmHg) was significantly higher than normotensive group (55.35 ± 2.16 mmHg) with \( P < 0.001 \). Furthermore, the comparison of OPP was performed between POAG and non-POAG groups. In hypertensive patients on anti-HT drugs, the mean in non-POAG category (60.16 ± 5.42 mmHg) was significantly higher than that of POAG category (48.67 ± 1.67 mmHg) with \( P < 0.001 \). In the normotensive group, the mean OPP in non-POAG category (55.35 ± 2.16 mmHg) was significantly higher than POAG category (46.23 ± 0.95 mmHg) with \( P = 0.0293 \).

Discussion

Glucoma is reported to be steadily increasing worldwide and particularly in South Central Asia. While studying glaucoma burden in Indian population, it was found that most of the glaucoma was advanced and undiagnosed at the time of...
Autoregulation of retinal blood flow and role of ocular perfusion pressure in healthy volunteers was studied by Riva et al. This later lower ocular perfusion pressure was found to be an independent risk factor for open angle glaucoma. It was reported that there is a role of systemic hypotension at night which in turn leads to low perfusion pressure of optic nerve head and increased risk of glaucoma. Hence, a positive correlation was found between blood pressure and IOP. Further, an ocular blood flow study also showed vascular abnormalities like altered resistivity index of Ophthalmic artery in glaucoma patients on Colour Doppler Imaging (CDI). The circadian dysfunction in systemic blood pressure, OPP and ocular blood flow was found to be an important risk factor for the severity of glaucoma.

In this case–control study of age- and sex-matched 103 hypertensives and 100 normotensive patients, we found that the mean IOP was higher in the hypertensive patients as compared to the control group. The Baltimore Eye survey reported that high IOP was found in patients with systemic hypertension and was a risk factor in the development of POAG. Evidence from the published literature and clinical trials suggests that OPP can also be linked to open-angle glaucoma. The OPP is the difference between IOP and SBP. Based on the evidence, low OPP is a risk factor for glaucomatous optic neuropathy in open-angle glaucoma. In our study, the mean OPP was higher in hypertensive group as compared to the normotensive group. This calculation using theoretical formulae in the office may not reflect the real status of OPP. As BP and IOP show diurnal variation hence single elevated or normal reading of BP or IOP may not represent the actual BP or IOP of an individual. The OPP in glaucoma is altered and shows fluctuations during 24-h circadian rhythm. It has detrimental effects on in the eyes with POAG who also have short-term IOP fluctuations during 24 h.

The association between POAG and systemic hypertension has been studied by various population-based studies published in literature. The Blue Mountain Eye Study and Egna-Neumarkt study found a positive correlation between open-angle glaucoma and systemic hypertension. But Deb et al. and Vijaya et al. found no significant association between the two.

In the Barbados Eye Study, systemic hypertension was found to be an important vascular risk factor, but it was not statistically relevant to the prevalence of glaucoma. Our study also did not find a significant association between open-angle glaucoma and systemic hypertension possibly due to small sample size. Patients with systemic hypertension on antihypertensive drugs may have DBP lower during the night as compared to day time. This nocturnal dip in the DBP can cause defective perfusion of optic nerve head leading to glaucoma. In our study, we calculated OPP in patients taking antihypertensive drugs and compared it with patients, not on antihypertensive drugs. We found that the mean OPP in patients taking antihypertensive drugs was significantly lower as compared to those not on antihypertensive treatment, and our results are similar to other studies reported in the literature.

In the present study, mean OPP in hypertensive patients with POAG was also compared to hypertensive patients without glaucoma. We found mean OPP was significantly lower in hypertensive patients with glaucoma. These findings provide evidence toward the role of OPP in the pathogenesis of POAG. We observed 9 cases of POAG in hypertensive patients out of which 8 were regularly taking anti-HT medication, while one was noncompliant for medication and hence was ignored from the comparison. These 8 POAG cases were compared with 2 POAG cases from the normotensive group; however, the comparison of OPP between two groups may not be justified due to small sample sizes, which was one of the shortcomings of this study. We could not measure 24-h BP to account for nocturnal hypotension in these patients, which was also the limitation of this study. Real incidence of open-angle glaucoma in hypertensive patients and its correlation with OPP can only be proved by continuous BP monitoring and recording of diurnal variation of IOP in longitudinal studies with large sample size. Although it is a study with a small sample size, it points toward the role of OPP in hypertensive patients in the development of glaucoma, and hence interdisciplinary management is the need of the hour.

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Conflicts of interest
There are no conflicts of interest.

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