

ASSOCIATION BETWEEN INTRAOCULAR PRESSURE, BLOOD PRESSURE, OCULAR PERFUSION PRESSURE AND PRIMARY OPEN ANGLE GLAUCOMA IN PATIENTS WITH SYSTEMIC HYPERTENSION

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ABSTRACT

Introduction: Glaucoma represents a group of diseases characterised by optic neuropathy which is consistent with remodelling of the connective tissue elements of the optic nerve head and with loss of neural tissue which leads to the eventual development of distinctive patterns of visual dysfunction. Although the intraocular pressure level is one of the primary risk factors for development of glaucoma, it does not have a role in the definition of the disease.

Aims: To evaluate the relationship between blood pressure, intraocular pressure and ocular perfusion pressure in patients with systemic hypertension.

Material and Methods: We studied 400 eyes of 200 hypertensive patients and compared them with 200 eyes of 100 non-hypertensive control subjects. We had aimed at finding the relation between blood pressure, intraocular pressure and ocular perfusion pressure in hypertensive patients and assessing the risk factors for developing primary open angle glaucoma in hypertensive patients.

Result:

- Mean Intra Ocular pressure in hypertensive patient is higher than that of non hypertensive patient's $P < 0.001$
- Mean ocular perfusion pressure is higher in hypertensive patients than non hypertensive patient's $P < 0.001$
- Intra ocular pressure has correlation with systolic and diastolic blood pressure.
- Intraocular pressure has correlation with Diastolic ocular Perfusion pressure and mean ocular perfusion pressure with mean ocular perfusion pressure having positive correlation with Diastolic blood pressure and negative correlation with glaucoma status.

Conclusion: A positive association exists between blood pressure and intraocular pressure, but similar association could not be established between blood pressure and primary open angle glaucoma. A significant association was seen between low diastolic blood pressure, low diastolic ocular perfusion pressure, low mean ocular perfusion pressure and glaucoma.

Keywords: Open Angle-Glaucoma, Blood Pressure, Ocular Perfusion Pressure and Hypertension.

INTRODUCTION

Essential hypertension remains a major modifiable risk factor for cardiovascular disease.¹ However, hypertension also has an impact on the ocular system which is manifested as hypertensive retinopathy. The microangiopathy of hypertension can result in end-organ damage including the retina and optic nerve. Glaucoma has also been found to be associated with blood pressure.

Glaucoma represents a group of diseases characterised by optic neuropathy which is consistent with remodelling of the connective tissue elements of the optic nerve head and with loss of neural tissue which leads to the eventual development of distinctive patterns of visual dysfunction. Although the intraocular pressure level is one of the primary risk factors for development of glaucoma, it does not have a role in the definition of the disease.

Primary open-angle glaucoma is a chronic, progressive optic neuropathy in adults which is characterized by loss of retinal ganglion cells and their axons; associated with open anterior chamber angle.²

The vascular theory suggests reduced blood flow to the optic nerve head as a risk factor for the development of glaucoma. Inadequate or unstable ocular blood supply causes ischemic damage and/or reperfusion injury to the optic nerve tissue and axons.

More recently, the role of blood pressure in the genesis of glaucoma has attracted attention, as it represents a clinically modifiable risk factor and thus provides the potential for new treatment strategies beyond intraocular pressure reduction. In systemic hypertension, chronically elevated blood pressure may result in arteriosclerosis, changes in the size of the precapillary arterioles, and capillary dropout leading to increased resistance to blood flow and, thus, reduced perfusion.³ Also high blood pressure could increase intraocular pressure by increased production of aqueous humor through elevated ciliary blood flow and capillary pressure and decreased aqueous outflow as a result of increased episcleral venous pressure. The interplay between blood pressure and intraocular pressure determines the ocular perfusion pressure, which regulates blood flow to optic nerve.

Aims:

- To evaluate the relationship between blood pressure, intraocular pressure and ocular perfusion pressure in patients with systemic hypertension
- To evaluate the risk of developing primary open angle glaucoma in patients with systemic hypertension
- To detect the prevalence of primary open glaucoma in patients with systemic hypertension
- To assess the relationship between glaucoma, suspect and ocular perfusion pressure

MATERIAL AND METHODS

- **Study design:** Institution based cross- Sectional observational study
- **Study duration:** One years and six months
- **Study place:** Out patients department (OPD) and glaucoma clinic of Regional Institute of Ophthalmology, Kolkata
- **Study population:** Patients visiting OPD and glaucoma clinic of RIO, Kolkata

- **Sample size:** 300 patients
 - Patients with diagnosed systemic hypertension – 200
 - Age and sex-matched patients without hypertension – 100
- **Inclusion criteria:**
 - i. Individuals >50 years of age
 - ii. Individuals with essential hypertension
 - iii. Individuals treated with antihypertensives for at least 1 year before the beginning of study
 - iv. Participants who signed informed consent
- **Exclusion criteria:**
 - i. Individuals with previous intraocular surgery, except uncomplicated cataract surgery
 - ii. Individuals with congenital ocular pathology
 - iii. Participants with angle closure glaucoma and other types of glaucoma
 - iv. Individuals with uveitis, corneal scarring, optic atrophy due to other causes
 - v. Participants with unconfirmed diagnosis of systemic hypertension
 - vi. Participants with prior diagnosis of primary open angle glaucoma
 - vii. Individuals with severe associated co morbidities (renal failure, congestive heart failure, sleep apnea, autoimmune diseases)
 - viii. Pregnant females
 - ix. Individuals with secondary hypertension
 - x. Diseases affecting visual field (pituitary tumors, demyelinating lesions, neurological causes) other than glaucoma
 - xi. Patients on medications known to affect visual field sensitivity. e.g. Chloroquine
 - xii. Subjects who were unable to co-operate with examination with incomplete information.

RESULT AND DISCUSSION

We studied 400 eyes of 200 hypertensive patients and compared them with 200 eyes of 100 non-hypertensive control subjects. We had aimed at finding the relation between blood pressure, intraocular pressure and ocular perfusion pressure in hypertensive patients and assessing the risk factors for developing primary open angle glaucoma in hypertensive patients.

We found that apart from high systemic blood pressure there are other factors contributing to the development of primary open angle glaucoma.

- In our study, there is no significant difference in glaucoma status between hypertensive and non-hypertensive patients. Patients who were effectively treated for systemic hypertension and had a significant reduction in diastolic blood pressure were found to have increased risk of- developing primary open angle glaucoma or glaucoma suspect.
- Many studies conducted to evaluate the association between hypertension and glaucoma status has failed to provide conclusive reports. Some of the findings of previous studies are as follows:
 - A strong association was found in poorly controlled hypertensive patients with 5.4% prevalence of open angle glaucoma than those with normal blood pressure (1.9% prevalence) in the Blue Mountain Eye Study. ⁴
 - Vijaya et al. in a study in south Indian rural and urban population found no association between systemic hypertension and primary open angle glaucoma. ⁵

- A bimodal relationship with “U” shaped curve was established between blood pressure and primary open angle glaucoma in the LALES which stated that there is an increased risk of developing primary open angle glaucoma in patients with both high and low blood pressure values. ⁶
- Our study showed a positive correlation between intraocular pressure and systolic blood pressure, but a negative correlation between intraocular pressure and diastolic blood pressure. We found that hypertensive patients had a higher mean intraocular pressure compared to non-hypertensive patients.
- Several population-based studies conducted to assess the correlation between intraocular pressure and blood pressure showed:
 - A positive correlation was found between blood pressure and intraocular pressure ($r = 0.39$ at 95% CI with $p = 0.005$) in the Beijing Eye Study, however there was no significant association of hypertension with glaucoma. ⁷
 - Zhao et al. supported the role of increased blood pressure in elevating intraocular pressure and thus playing a role in development of primary open angle glaucoma. ⁸
 - The Beaver Dam Eye Study conducted to assess the relation between change in systemic blood pressure and intraocular pressure showed that with every 10 mmHg rise in systolic blood pressure there was a 0.21 mmHg rise in intraocular pressure and for every 10 mmHg rise in diastolic blood pressure there was a 0.43 mmHg rise in intraocular pressure. ⁹
- A dip in diastolic blood pressure as a result of antihypertensives or even in healthy participants is believed to play a role in glaucoma pathogenesis by Kwon et al. ¹⁰
- Although raised intraocular pressure is considered to be an important risk factor for development of primary open angle glaucoma, several other vascular factors have also been identified. The main pathological mechanism is hypoperfusion of the optic nerve head. Thus, several studies have attempted to find a relationship between ocular perfusion pressure and glaucoma status.
- Our study showed that hypertensive patients had higher mean ocular perfusion pressure in comparison to non-hypertensive patients. It is also seen that chronic hypertensive subjects on long term treatment had reduced systolic ocular perfusion pressure, diastolic ocular perfusion pressure and mean ocular perfusion pressure. Intraocular pressure was found to be negatively correlated with systolic ocular perfusion pressure, diastolic ocular perfusion pressure and mean ocular perfusion pressure in our study.
- Reports of previous studies are as follows:
 - Gore et al. in an attempt to find the relationship between intraocular pressure and ocular perfusion pressure found that intraocular pressure had a negative correlation with systolic ocular perfusion pressure, diastolic ocular perfusion pressure and mean ocular perfusion pressure. ¹¹
- In our study we have found a negative correlation between mean ocular perfusion pressure and glaucoma status, which indicates that low mean ocular perfusion pressure is associated with increased incidence of glaucoma.
- Other studies supporting our finding are:
 - Zheng et al in the Singapore Malay Eye Study showed that systemic hypertension was protective against open angle glaucoma because of the fact that hypertensives had higher ocular perfusion

pressure than normotensives.¹² They also said that diastolic ocular perfusion pressure and mean ocular perfusion pressure were significantly associated with risk of glaucoma development and progression.

- In the Singapore Malay Eye study, 32.1% and 35.1% of open angle glaucoma cases fell within the lowest quartile of mean ocular perfusion pressure (<46 mm Hg) and diastolic ocular perfusion pressure (<56 mm Hg), respectively.¹²
- In our study, 75% of the patients diagnosed with primary open angle glaucoma had diastolic ocular perfusion pressure <55mmHg and mean ocular perfusion pressure <50mmHg. Thus, low diastolic ocular perfusion pressure and low mean ocular perfusion pressure is a strong predictor of glaucoma.
- Studies in accordance with our finding are:
 - The Barbados Eye study showed that low diastolic ocular perfusion pressure and low mean ocular perfusion pressure are independent risk factors for developing primary open angle glaucoma.¹³ Ocular perfusion pressure depends on a complex mechanism that is maintained by a balance between blood pressure and intraocular pressure. Vascular dysregulation leads to alteration of this balance and thus causing disruption in ocular perfusion. This mechanism has been proposed to be the underlying cause for glaucomatous optic neuropathy.¹⁴

On the other hand, we found a positive correlation between mean ocular perfusion pressure and diastolic blood pressure which indicate that low diastolic blood pressure is associated with low mean ocular perfusion pressure, which can indirectly affect ocular blood flow and thus, lead to glaucomatous optic neuropathy. Low diastolic blood pressure may be due to the result of long-term anti-hypertensive treatment or nocturnal dip in blood pressure. In our study, glaucoma among the hypertensive patients were noted among those with a prolonged duration of anti-hypertensive medication. Zhao et al. stated that treated or overtreated hypertensive patients can have normal or low blood pressure but an elevated risk of developing primary open angle glaucoma.¹⁵ This finding was consistent with our study which showed that hypertensive patients well-controlled on medications had a lower diastolic blood pressure, lower diastolic ocular perfusion pressure, lower mean ocular perfusion pressure, but higher intraocular pressure and increased risk of developing primary open angle glaucoma.

CONCLUSION

- No significant difference in glaucoma status between hypertensive and non-hypertensive subjects, with 6% of the hypertensive and 4% of the non-hypertensive subjects being diagnosed with primary open angle glaucoma and 11% of hypertensive and 7% of non-hypertensive subjects being diagnosed as glaucoma suspects.
- A positive association exists between blood pressure and intraocular pressure, but similar association could not be established between blood pressure and primary open angle glaucoma.
- A significant association was seen between low diastolic blood pressure, low diastolic ocular perfusion pressure, low mean ocular perfusion pressure and glaucoma.

It can be said that glaucoma is a multifactorial disease and not just the outcome of raised intraocular pressure. Vascular factors have a significant role in pathogenesis of glaucoma. Both high and low blood pressure may be associated with development glaucoma by different mechanisms. This can be

explained by the fact that arteriosclerotic changes in long standing hypertension leads to reduced caliber of capillary walls and reduced perfusion of optic nerve head.

Microangiopathy of hypertension can cause damage to end organs like retina and optic nerve head. On the contrary reduced blood pressure due to long standing treatment or night time dosage of antihypertensive can also cause a drop in ocular perfusion pressure and thus ischemic injury of the optic nerve head.

Thus, it is important to maintain a steady ocular perfusion pressure irrespective of hypertension status. It is essential to monitor night time dosage of anti- hypertensive medications, particularly in patients susceptible to develop glaucoma.

However further studies are recommended on the effect of antihypertensive medications and their duration of treatment on glaucoma development and progression.

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TABLE**Distribution of Ocular Perfusion Pressure****Table 1 showing distribution of SOPP, DOPP and MOPP in hypertensive (n=200) and non-hypertensive (n=100) patients**

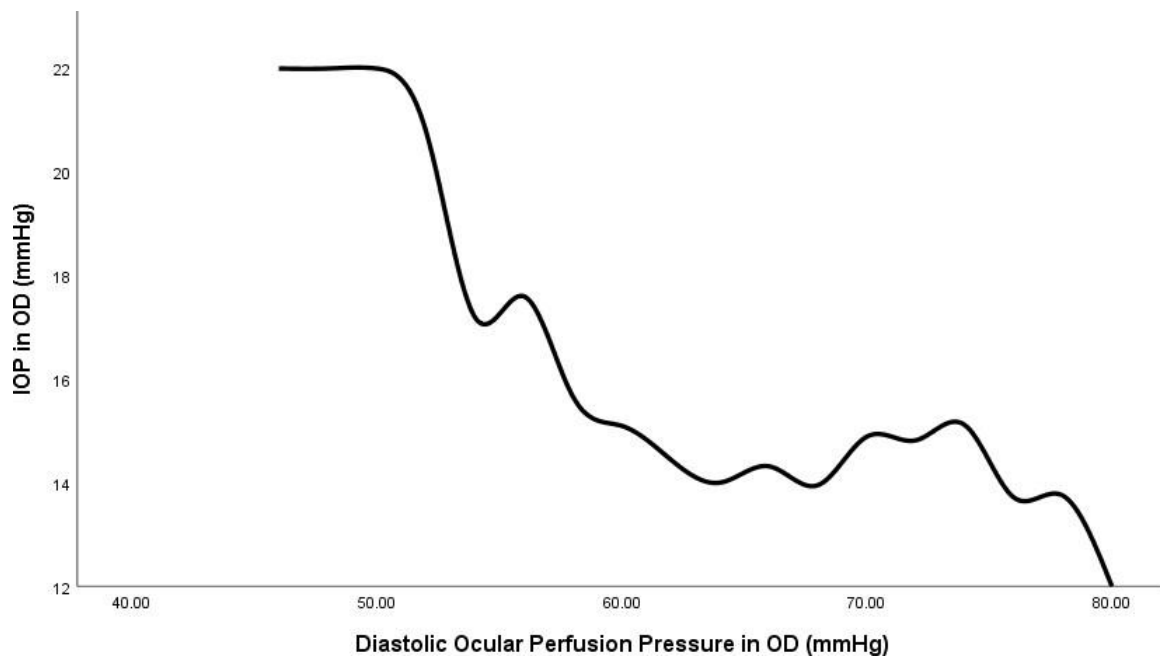
Variable	Hypertensive (n= 200)		Non-hypertensive (n =100)		P value ¥
	OD	OS	OD	OS	
Mean SOPP (mmHg) ± SD	127.55 ± 8.03	127.56 ± 8.2	111.78 ± 6.8	111.68 ± 6.8	<0.001
Median SOPP (mmHg)	128	128	112	112	
Mean DOPP (mmHg) ± SD	67.02 ± 6.7	67.03 ± 6.7	63.12 ± 4.8	63.02 ± 4.8	<0.001
Median DOPP (mmHg)	68	68	64	64	
Mean MOPP (mmHg) ± SD	58.13 ± 4.2	58.14 ± 4.3	52.89 ± 3.2	52.82 ± 3.2	<0.001
Median MOPP (mmHg)	58.22	58.22	53.33	53.11	

Prevalence of Primary Open Angle Glaucoma and Glaucoma Suspect

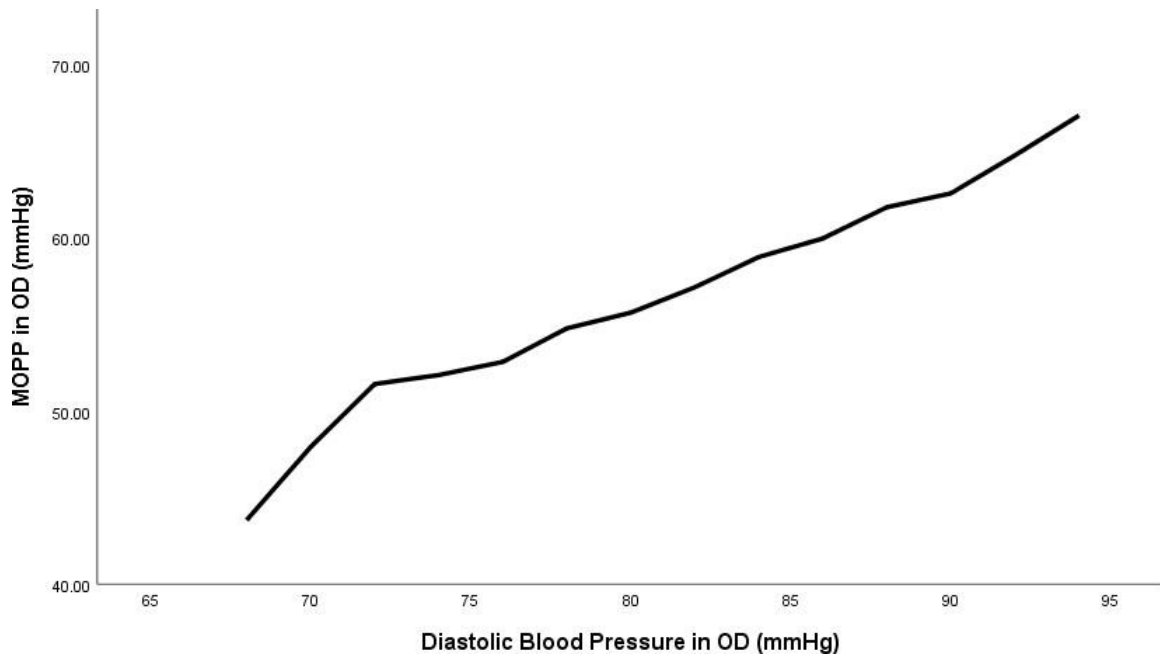
Table 2 showing comparison of glaucoma status between hypertensive (n=200) and non-hypertensive patients (n=100)

Variable	Hypertensive (n=200)		Non-hypertensive (n=100)		P value [¥]
	n	%	n	%	
No glaucoma	166	83%	89	89%	0.11
Glaucoma suspect	22	11%	7	7%	
Primary Open Angle Glaucoma	12	6%	4	4%	

Correlation between Ocular Perfusion Pressure and Intraocular Pressure



Line diagram showing correlation between intraocular pressure and DOPP in right eye (n=300)



Line diagram showing relation between mean ocular perfusion pressure and diastolic blood pressure in right eye (n=300)