



## Original Research Article

## Study on progression of primary open angle glaucoma in patients with maintained target intraocular pressure

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Systolic Ocular Perfusion

Pressure(SOPP)

Diastolic Ocular Perfusion

Pressure(DOPP)

Mean Ocular Perfusion

Pressure(MOPP)

## ABSTRACT

**Purpose:** To study progression of primary open angle glaucoma in patients with maintained target intraocular pressure.**Materials and Methods:** This was a prospective observational study comprising 30 diagnosed patients of primary open angle glaucoma on maintained target intraocular pressure conducted for a period of 2 year. Patients underwent complete ophthalmic examination including IOP, optic disc evaluation & visual fields. Systolic and diastolic blood pressure was measured with sphygmomanometer using adult cuff size. Systolic, diastolic & mean ocular perfusion pressure ocular perfusion pressure were calculated. Patients were examined at baseline then at 12 months then at next 12 months. Progression of glaucoma was assessed on the basis of changes in VF's & optic disc between baseline and final follow at 2 years. Data analyzed using standard statistical technique and a probability value ( ' p ' value) of < 0.05 was considered as statistically significant.**Results:** Mean age of study participants was 54±0.07 years ,M:F ratio was 1.5:1. Progressive patients showed significantly changes in optic disc cupping C:D ratio {0.67±0.11} at baseline to {0.74±0.13} final follow up (p<0.05) and in visual fields in MD {-2.1±0.83} at baseline to {-7.0±1.3} final follow up (p<0.05) ,PSD {-1.3±0.6} at baseline to {-5.8±1.3} final follow up (p<0.05) as compared to non progressive group. DBP, DOPP and MOPP were significantly lower in progressive group as compared to non-progressive group.**Conclusions:** Low DBP, low MOPP, and low DPP are risk factor for primary OAG progression with maintained target intraocular pressure, providing further evidence of a vascular mechanism in glaucoma pathogenesis© 2019 Published by Innovative Publication. This is an open access article under the CC BY-NC-ND license (<https://creativecommons.org/licenses/by/4.0/>)

## 1. Introduction

Glaucoma is defined as a chronic progressive optic neuropathy involving retinal ganglion cell death indeed leading to visual field loss.<sup>1</sup> The only modifiable risk factor for POAG is considered to be raised IOP. Glaucoma treatment was initially based mainly on IOP reduction to a level at which no additional damage is expected to occur. This level was called as the Target IOP.

Recently it has been established with evidence that POAG is secondary to optic nerve head hypoperfusion and autonomic dysfunction. Vascular factors, can

causes reduced perfusion of the optic disc which leads to glaucomatous optic disc damage.<sup>2-4</sup> Factors for the prevalence, incidence, and progression of glaucoma are low BP, BP variability, nocturnal hypotension, and low or fluctuating ocular perfusion pressures (OPP) as suggested in large epidemiological surveys<sup>5-7</sup>

The present study has been conducted with the view of adding significantly to the current body of evidence by providing a collective report on associations of various potential risk factors with the progression of POAG on maintained target intraocular pressure.

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## 2. Objectives

1. To study the clinical profile of patient with primary open angle glaucoma in patients with maintained target intraocular pressure.
2. To evaluate the progression of glaucoma by optic disc evaluation and visual fields by automated perimetry in patient with maintained target intraocular pressure.
3. To study the factors responsible for progression of POAG in patients with maintained target intraocular pressure.

## 3. Materials and Methods

This was a prospective observational study was done on 30 patients (60 eyes) of POAG and normal tension glaucoma patients for a duration of two years (August 2016 to September 2018) after obtaining the clearance from institutional ethics committee. Informed consent was taken from all patients.

The inclusion criteria were all the patients of primary open angle glaucoma on treatment with maintained target intraocular pressure. The exclusion criteria were all patients of primary open angle glaucoma on treatment without maintained target intraocular pressure, all secondary glaucoma and all other diseases leading to changes in retinal nerve fibre layer condition and field defects

Preliminary demographic data of patients were noted. A brief history of hypertension, heart disease, hemodynamic crisis (acute blood loss following trauma, surgery etc.), family history of glaucoma, and migraine were noted.

The ocular examination included visual acuity (Snellen's chart), refraction, tonometry (applanation), diurnal variation, slit lamp examination, fundus examination including optic disc evaluation (+90D/direct ophthalmoscopy), Optic disc cupping, neuroretinal rim thinning, disc hemorrhage, peripapillary atrophy, focal notching, nerve fiber layer defects, and lamellar dot sign were examined. Visual Field evaluation was done using Humphrey field analyzer (30-2). A second visual field report of every patient was taken for analysis accounting for consistency of findings and the patient's learning curve. Visual field defects were analyzed using Anderson's criteria and graded accordingly

### 3.1. Blood pressure

Single measurement of BP was taken for all the subjects in the right upper arm in sitting position using a mercury sphygmomanometer (auscultatory technique using the first and fifth phases of the Korotkoff sounds as per the American Heart Association BP measurement recommendation)

Optic disc perfusion pressure calculated by formula

Mean ocular perfusion pressure= $\frac{2}{3}$  Mean arterial pressure-IOP

(MAP=Diastolic blood pressure- $\frac{1}{3}$ Pulse pressure)

Pulse pressure=Systemic blood pressure-Diastolic blood pressure)

### 3.2. Systolic and diastolic ocular perfusion pressure calculated

Systolic ocular perfusion pressure=SBP-IOP

Diastolic ocular perfusion pressure=DBP-IOP

30 Primary open angle glaucoma patients with systemic hypertension on treatment and on maintained target intraocular pressure are being evaluated for progression on the basis of optic disc changes, visual fields between baseline and final follow up.

## 4. Results

The present study was conducted on 60 eyes of 30 patients of primary open angle and normal tension glaucoma who were on maintained target intraocular pressure. Mean age in study participants was  $54 \pm 0.07$  years

Age wise distribution in study patients

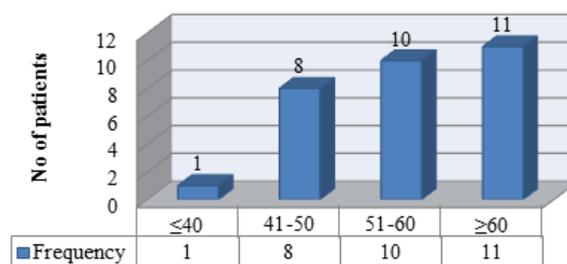


Fig. 1: Showing age- wise distributions in study patients

1 patient (3.3%) was below 40 years of age, 8 patients (26.7%) between 41-50 year age group, 10 patients (33.33%) between 51-60 year of age group and 11 patients (36.7%) more than 60 years age group, shows that POAG is more prevalent in older age group.

Gender wise distribution in study patients

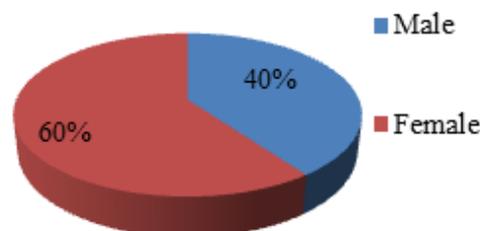


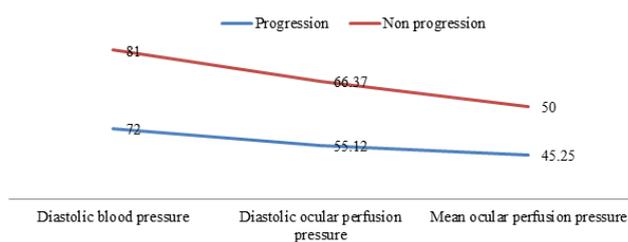
Fig. 2: Gender wise distributions of patients

**Table 1:** Assessment of progression of glaucoma in study patients

Variables		Progression	Nonprogression
Mean of MD	Baseline	-2.1±0.83	3.6±3.3
	Final follow up after 12 month	-7.0±1.3	2.7±3
	P value (paired t)	0.01	0.19
Mean of PSD	Baseline	-1.3±0.6	3.5±2.4
	Final follow up after 12 month	-5.8±1.3	2.8±1.1
	P value (paired t)	0.01	0.14
Mean of C:D ratio	Baseline	0.67±0.11	0.48±0.04
	Final follow up after 12 month	0.74±0.13	0.51±0.04
	P value (paired t)	0.01	0.6

Out of 30 patients, 18 patients (60%) were male and 12 patients (40%) were female, making the sex ratio 1.5:1.

Significant progression in terms of changes in mean cup; disc ratio, mean of mean deviation and mean of patterned standard deviation was observed in progressive group with p value of <0.01 for each (significant) while non progressive group showed not significant results with p value of 0.6, 0.19 and 0.14 respectively.

**Fig. 3:** Correlation of DBP, DOPP & MOPP between progression and non progression

Statistical analysis showed no significant difference between mean age groups of progressive and non progressive patients ( $p = 0.66$ ). Also, there was no statistically significant difference of systolic blood pressure and systolic ocular perfusion pressure of progressive and non progressive patients with p value of 0.8 and 0.9 (non significant) respectively at baseline as well as at final follow up.

Significantly low diastolic blood pressure, diastolic ocular perfusion pressure and mean ocular perfusion pressure was found in progressive patients as compared to non progressive patients with p value of <0.01 each (significant) at baseline as well as at final follow up.

Larger diurnal fluctuations were observed in progressive patients as compared to non progressive patients with p value of 0.03 (significant) at baseline as well as at final follow up.

#### 4.1. Statistical analysis

Descriptive statistics (mean and SD) were calculated for the variables. Statistical analyses were performed, test of significance (unpaired T test and paired t) wherever applicable, were applied, ( $P < 0.05\%$ ) was taken significant at 95% Confident interval

## 5. Discussion

The theories that explain the pathogenesis Glaucoma are mechanical and vascular theories, explained by structurally weak lamina cribrosa and vasospasm compromising optic nerve head perfusion.

#### 5.1. Assessment of progression of glaucoma

Significant visual fields deterioration was observed in group with progression between baseline and at follow up whereas, in non progression group non significant visual fields deterioration was observed. Significant increase in cupping between baseline and follow up whereas non progressive group did not show significant increase in cupping. Similarly, Bhartiya S et al<sup>88</sup> (2010) found that a detailed evaluation by slit lamp biomicroscopic techniques of optic disc and nerve fibre layer provides the clinician with an excellent method for early detection of glaucoma and in monitoring its progression.

#### 5.2. DBP with glaucoma progression

The present study demonstrated lower DBP in progression patients as compared to non progression patients. Thus it can be concluded that DBP is a risk factor for POAG and can lead to optic disc hypo perfusion and thus is a key factor in the pathogenesis and progression of POAG. This was consistent with Pache M et al<sup>9</sup> (2006) who found hypotension, and in particular a nocturnal decrease in blood pressure, as an important risk factor for P OAG. Dong L et al<sup>10</sup> (2007) in early manifest glaucoma trial concluded that lower DBP in patients with lower baseline IOP was associated with faster progression to OAG. Capriol J et al<sup>11</sup> (2010) concluded that decreases in perfusion pressure and blood pressure have been associated with glaucoma.

**Table 2:** Comparisons of risk factors between progressors and nonprogressors

Variables		Progression	Non progression	P value
Mean age		54.83±10.80	52.75±9.43	0.66
Mean systolic blood pressure	Baseline	133.83±9.9	132.5±4.62	0.8
	Final follow up	127.5±7.53	127.2±4.6	0.9
Mean diastolic blood pressure	Baseline	71.66±3.89	80±0.00	<0.01
	Final follow up	72±3.40	81±3.89	<0.01
Mean systolic ocular perfusion pressure	Baseline	117.62±8.84	118±3.87	0.8
	Final follow up	113.62±7.35	114±3.57	0.8
Mean diastolic ocular perfusion pressure	Baseline	53.87±3.32	64.25±3.33	<0.01
	Final follow up	55.12±1.11	66.37±1.02	<0.01
Mean of mean ocular perfusion pressure	Baseline	45.04±3.68	50.5±1.03	<0.01
	Final follow up	45.25±2.32	50±0.00	<0.01
Mean diurnal variation	Baseline	7.29±1.04	6.56±0.72	0.03
	Final follow up	7.08±1.01	6.37±0.61	0.03

Randomized clinical trials also suggested that low BP is associated with risk and progression of glaucoma.

### 5.3. Diastolic ocular perfusion pressure and glaucoma progression

The present study concluded that, glaucoma progression was associated with low diastolic ocular perfusion pressure. This was consistent with, Leske MC et al<sup>12</sup> (2002) in The Barbados Eye study found a low DOPP had an increased risk of developing and progressing OAG. Chung J et al<sup>13</sup> (2010) in The Los Angeles Latino Eye Study (LALES) reported that low DOPP associated with an increased prevalence of OAG.

Aggressiveness of anti-hypertensive treatments associated with pro gression of POAG. Mechanism may be reduction in diastolic blood pressure associated with antihypertensive therapy with exacerbation in nocturnal dipping of OPP. In the Thessaloniki Eye Study<sup>14</sup>, low DOPP was associated with an increased risk for POAG in subjects undergoing antihypertensive treatment. Rotterdam Eye Study also revealed that lower diastolic perfusion pressure in persons taking antihypertensive medication was associated with the higher prevalence of high tension OAG.

### 5.4. Mean ocular perfusion pressure and glaucoma progression

Low mean ocular perfusion pressure was associated with glaucoma progression. This was consistent with, Connel A M et al<sup>15</sup> (1995), in the Barbados Eye Studies revealed that glaucoma progression was associated with lower MOPP, the relative risk for developing OAG was 2.6. Leske MC et al<sup>12</sup> (2002) in The Barbados Eye study found that Individuals with a low mean OPP had an increased risk of developing and progressing glaucoma.

### 5.5. Diurnal fluctuations

In present study, we found larger diurnal variation was found associated with progression of glaucoma. This was correlated with, Asrani S G et al<sup>16</sup> (2000) found large fluctuations were found to be an independent risk factor for glaucoma progression. Choi et al<sup>17</sup> found a positive association between larger circadian MOPP fluctuations and more significant visual field defects

## 6. Conclusion

This study demonstrated various vascular risk factors to be associated with glaucoma progression in patients with systemic hypertension on treatment with maintained target IOP including

1. Low diastolic Blood pressure //
2. Decreased diastolic ocular perfusion pressure
3. Decreased mean ocular perfusion pressure
4. Larger diurnal fluctuations

OPP is a important risk factor for glaucoma onset and progression, and has found to be a modifiable risk factor and treatment target in glaucoma. OPP is more contributed by IOP and diastolic BP than does with systolic BP It is important to monitor 24-hour IOP and BP measurements as it prov ides more detailed assessments than single daytime measurements.

Hence risk of glaucoma progression is connected with low DBP. So the antihypertensive prescribed should be chosen cautiously.

### 6.1. List of abbreviations

POAG: Primary open angle glaucoma, NTG: Normal tension glaucoma, OHT: Ocular hypertensive, IOP: Intraocular pressure, OD: Optic disc, C: D: Ratio cup: disc ratio, NRR: Neuro retinal rim, RNFL: Retinal nerve fibre layer, AP: Automated perimetry, TP: Target pressure, WHO: World health organization, DM: Diabetes mellitus,

HTN: Hypertension, CAD: Coronary artery disease, UCVA: Uncorrected visual acuity, BCVA: Best corrected visual acuity, MD: Mean deviation, SD: Standard deviation, PSD: Pattern standard deviation, CPSD: Corrected pattern standard deviation, Db : Decibels, RE: Right eye, LE: Left eye, mmHg: Millimetres of mercury, PR: Pulse rate, BP: Blood pressure, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, MAP: Mean arterial pressure, SOPP: Systolic ocular perfusion pressure, DOPP: Diastolic ocular perfusion pressure, MOPP: Mean ocular perfusion pressure, OPP: Ocular perfusion pressure,

## 7. Source of Funding

None.

## 8. Conflict of Interest

None.

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