

# Identification of potential predictive vascular indicators for primary open angle glaucoma- a case control study

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## Abstract

**Introduction:** Glaucoma is the second leading cause of irreversible blindness worldwide and recently a vascular mechanism has been postulated in the pathogenesis of glaucomatous optic nerve damage but the relationship of the various hemodynamic factors and open angle glaucoma is still controversial. **Aim:** To compare the intraocular pressure and the different vascular indices among cases and controls; to determine their relationship with primary open angle glaucoma. **Settings and Design:** Hospital based case control study. **Methods and Material:** The study was undertaken from November 2014 to October 2015 in a tertiary care centre with 200 participants above 40 years comprising of 100 cases of primary open angle glaucoma and a similar number of randomly selected age and sex matched healthy controls. All underwent a detailed comprehensive ocular examination. The blood pressure was measured in each and the variables like systolic - diastolic perfusion pressures, mean arterial and mean ocular perfusion pressures were calculated using the formulas. **Results:** Amongst all vascular factors studied, diastolic blood pressure, mean ocular perfusion pressure and intraocular pressure were extremely significant among cases as compared to controls. Those having higher intraocular pressure had higher values of systolic, diastolic and mean arterial pressures and intraocular pressure had a positive correlation with these pressures. **Conclusion:** The mean ocular perfusion pressure was very much lower in cases than in controls and the difference too was highly significant and hence we conclude that along with high intraocular pressure, a vascular mechanism is there behind the occurrence of primary open angle glaucoma.

**Keywords:** Glaucoma, vascular mechanism, Pulse pressure

## Introduction

Worldwide, glaucoma is the second leading cause of irreversible blindness, affecting more than 67 million people [1]. Hypertension is a disease which is becoming increasingly common in the developing countries. Blood pressure influences optic nerve perfusion. Pulse pressure (difference between systolic blood pressure and diastolic blood pressure) also is indicated in the pathology of optic nerve damage as higher pulse pressure may impair ocular autoregulation and due to this impaired autoregulation, the vessels may not be able to respond to low diastolic blood pressure in order to maintain perfusion, which may result in ischaemic insult to the optic nerve. The literature on the association between systolic or diastolic blood pressure

(SBP, DBP) and glaucoma is confusing with some population-based studies showing an association and others not [2-5]. Vascular mechanism has been postulated in the pathogenesis of glaucomatous optic nerve damage. Various indices [like mean arterial pressure, systolic and diastolic perfusion pressures (SPP, DPP) and mean ocular perfusion pressure (MOPP)] have been indicated but their relationship with glaucoma is not well understood [6-7].

Hence, understanding the relationship between these parameters is important to determine the risk factors influencing open angle glaucoma. The present study was undertaken in a tertiary care centre of central Gujarat to compare the intraocular pressure and the different vascular factors among cases with primary open angle glaucoma (POAG) and controls.

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## Materials and Methods

**Study area:** This study was carried out in the Department of Ophthalmology in a tertiary health care centre in Central Gujarat.

**Study design, study population and study duration:**

A case control study was done among 200 subjects comprising of 100 cases of Primary open angle glaucoma and 100 randomly selected age and sex matched healthy controls (participant's relatives presenting to the Department). The study period was from November 2014 to October 2015.

**Operational definitions:** The cases were defined as the patients of primary open angle glaucoma including the ocular hypertension and the normal tension glaucoma [8].

**Sample size determination:** Sample size was calculated based on previous case-control study conducted by Reza Zarei et al in 2011[9]; using G Power software version 3.1.9.2.

Following inputs were provided; effect size=0.43,  $\alpha$ =0.05 and power of 85 %, the calculated sample size was 196 (with 98 in each group). So, we rounded off to 200 participants with 100 cases and 100 controls.

**Inclusion criteria:** Adult patients of POAG above 40 years (treated or untreated) attending OPD's on Monday, Wednesday, Friday and giving written informed consent were included in the study as cases. Relatives of the cases were selected as controls after taking consent.

**Exclusion criteria:** Patients with angle closure glaucoma, secondary glaucoma, corneal scarring or opacity and other causes of optic atrophy were excluded.

**Measurement methods:** A detailed history including family history of glaucoma and history of any medications, past medical illness or ocular diseases was taken. A comprehensive ocular examination including best corrected visual acuity (BCVA) using an illuminated Snellen's chart, with the patient seated at 6 meters distance, torch light and slit lamp examination-to

rule out anterior segment pathology, gonioscopy using Goldmann 3 mirror lens was performed for all cases of open angle glaucoma using the standard techniques[8]. Indentation tonometry was done by Schiotz tonometer to measure intra ocular pressure using standard technique [8]. Fundus examination was carried out by direct ophthalmoscope followed by a slit lamp biomicroscopic evaluation with 78D lens to evaluate posterior pole including the optic disc.

Autoperimetry- using static autoperimeter model Medmont M700 for visual field assessment. Blood pressure measurement was done by mercury sphygmomanometer instrument using the auscultatory technique with the patient in sitting position after resting for 5 minutes.

**Definition of predictive variables:** The systolic perfusion pressure (SPP) and diastolic perfusion pressure (DPP) were calculated by subtracting the intraocular pressure (IOP) from the systolic blood pressure (SBP) and diastolic blood pressure (DBP) respectively.

Mean arterial pressure (MAP) =  $DBP + 1/3(SBP - DBP)$ .  
Mean ocular perfusion pressure (MOPP) =  $2/3[\text{mean arterial pressure (MAP)} - \text{intraocular pressure (IOP)}]$ [10].

**Data management:** Data was collected using structured data collection proforma. Collected data was entered into Microsoft Excel worksheet.

Descriptive statistics like mean and standard deviation (SD) were calculated in Microsoft Excel Worksheet. Analytical Statistics like student's 't' test, Pearson's correlation coefficient, 95% confidence interval (CI) and  $r^2$  was done using Medcalc Software version 11.5.0. A p-value of less than 0.05 was considered statistically significant.

**Ethical concern:** Approval was obtained from the Institutional ethics committee before start of the study. A written and informed consent was obtained from all the participants before enrolment in the study. All measurements on the patients were done ensuring adequate privacy. Data confidentiality was maintained by keeping files password protected.

## Results

The Mean $\pm$ SD age among cases was 51.5 $\pm$ 7.3 years and that among controls was 50.9 $\pm$ 5.6 years. Amongst the cases 61% were males and among controls also 60% males. Since the age and sex distributions of the case and control groups were matching each other (difference < 5%), both groups were comparable. Out of a total of 100 cases POAG accounted for 56 %, OHT accounted for 25 % and NTG accounted for 19%.

Amongst all vascular factors studied, DBP, MOPP and IOP were significantly higher among cases as compared to controls (Table 1). Moreover, we observed that patients having IOP in higher range also had higher values of SBP, DBP and MAP as depicted in Figure 1.

So, to find out correlation between IOP, blood pressure and ocular perfusion pressures, correlation coefficients were calculated. As shown in Table 2, IOP had a positive correlation with SBP, DBP and MAP; and was statistically significant. However, IOP had a negative correlation with SPP, DPP and MOPP; although the findings were not statistically significant.

**Table-1: Comparison of vascular factors and IOP among cases and controls.**

Vascular factors	Cases (N=100) Mean±SD	Controls (N=100) Mean±SD	t – test	p – value
SBP	127.8±15.9	125.7±15.6	0.94	0.34
DBP	83.7±9.9	80.6±9.9	2.2	0.02*
MAP	98.4±11.3	95.6±11.3	1.75	0.08
SPP	105.3±15.6	108±15.6	1.2	0.2
DPP	61.2±9.8	63.2±9.9	1.4	0.1
MOPP	50.6±7.5	78.3±11.4	20.2	0.0001*
IOP	22.5±4.1	17.3±3.2	9.9	0.0001*

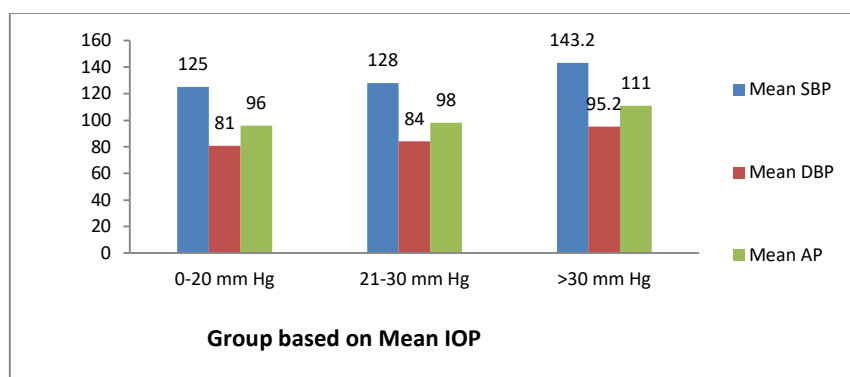
\*statistically significant, SD-Standard Deviation

SBP-Systolic blood pressure; DBP-Diastolic blood pressure; MAP-Mean arterial pressure; SPP-Systolic perfusion pressure; DPP- Diastolic perfusion pressure; MOPP-Mean ocular perfusion pressure; IOP- Intra ocular pressure

**Table-2: Correlation of IOP and other vascular factors among cases.**

Comparison	Correlation Coefficient(r)	p-value	95% C.I. of r	r <sup>2</sup>
IOP vs SBP	0.2124	0.0339*	0.01677 to 0.3924	0.04511
IOP vs DBP	0.2469	0.0133*	0.05302 to 0.4228	0.06095
IOP vs MAP	0.2406	0.0159*	0.04642 to 0.4173	0.05788
IOP vs SPP	-0.02603	0.7972	-0.2213to0.1713	0.00068
IOP vs DPP	-0.1006	0.3191	-0.2913to0.09771	0.01012
IOP vs MOPP	-0.07185	0.4775	-0.2645 to 0.1264	0.00516

\*statistically significant, CI – Confidence Interval; SBP-Systolic blood pressure; DBP-Diastolic blood pressure; MAP-Mean arterial pressure; SPP-Systolic perfusion pressure; DPP- Diastolic perfusion pressure; MOPP- Mean ocular perfusion pressure; IOP- Intra ocular pressure.



\*SBP-Systolic blood pressure; DBP-Diastolic blood pressure; MAP-Mean arterial pressure

**Figure-1: Comparison of mean blood pressures amongst IOP groups**

## Discussion

On detailed analysis amongst cases, we found that all had significantly lower MOPP compared to controls and that DBP, MOPP & IOP were having statistically significant p-values among cases compared to controls. Mean IOP was higher in cases than amongst the controls.

Mean BP and Mean IOP was higher among cases as compared to controls in the present study. Similar findings were observed in Barbados Eye study and Beaver Dam Eye Study [3,11]. Blue Mountain Eye Study found that a higher SPP was associated with OAG risk (OR,1.09; p=0.05) and a higher DPP was associated with reduced risk of OHT (OR,0.78; p=0.0008) [12]. In Singapore Maleyeye study, SBP was not associated with increased risk of POAG[13]. This difference in study results may be partially explained by the difference in criteria used to define hypertension, the inclusion and exclusion criteria used for OAG, NTG and OHT cases, the impact of IOP or blood pressure lowering therapy, or the variable susceptibility of people of different ancestries to OAG (Confounders).

In the present study, p value of DPP was not statistically significant though it was lower in cases than in the controls, and it showed to have a negative correlation (r=-0.1006) although this correlation too was not statistically significant (p=0.3191). This finding of the present study was not in agreement with the finding of the Baltimore Eye Survey and Barbados Eye Study where a lower DPP was associated with an increased risk of POAG [3,4]. The Egna-Neumarkt Study has shown a positive correlation between systemic blood pressure (SBP) and IOP; an association was also found between diagnosis of POAG and systemic hypertension; lower DPP was associated with a marked progressive increase in frequency of glaucoma in that study[5].

In the present study, SBP, DBP and MAP were found to have statistically significant p values and had positive correlation coefficient with IOP as was also found in Blue Mountain Eye Study, Taiwan Study, Egna-Neumarkt Study and Latino Study which too showed that IOP was higher in persons with higher blood pressure; this relationship was significant for both SBP and DBP (p value<0.01) and was independent of age[5, 12-15]. It was observed that MOPP was very much lower in cases than in controls and that the difference too was also extremely significant, however its correlation with POAG was not predictive. This could be because the calculation of mean OPP was done using

theoretical formulas which may not reflect the real physiological status of ocular perfusion. Direct measurement could result in different outcomes. Blood pressure and IOP are both influenced by diurnal variations which were acknowledged; therefore, having a single elevated/ normal blood pressure or IOP reading may not be representative of an individual's true blood pressure or IOP status. In addition, patients were not followed for the development of progression of glaucoma.

## Conclusion

So, it can be concluded that along with high IOP, a vascular mechanism is there behind the occurrence of POAG and hence the vascular predictors should be measured regularly in all patients of POAG in routine practice. Increased IOP and high blood pressure was observed in cases of POAG as compared to controls.

Vascular factors like DBP and MOPP were found to be significantly associated with cases of POAG compared to controls while raised IOP showed positive correlation with SBP, DBP and MAP. DBP and MOPP appear to be predictors of POAG and hence should be measured regularly in all patients of POAG in routine practice.

## What this study adds to existing knowledge?

Currently intraocular pressure is the only risk factor of glaucoma that can be modified with medical and surgical intervention. Evaluation of the observations from the present study in light of available literature it can be conceived that by maintaining blood pressure and ocular perfusion pressure at physiologic levels on a long-term basis, there might be reduction in the risk of development of glaucomatous optic nerve damage.

## Authors Contribution

**Dr. Stuti V Juneja:** Conceived and designed the idea, manuscript writing, drafting, critically revising and final approval.

**Dr. Aanal Shah:** Carried the clinical study and collection of data and analysis.

**Dr. N N Pandya:** Data analysis, supervision and revision.

**Dr. Parag Chavda and Dr.Kedar Mehta:** Statistical Analysis and Manuscript editing.

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