Primary Open Angle Glaucoma and Ocular Perfusion Pressure in Patients with Hypertension and Those Without Hypertension Attending Federal Medical Centre, Umuahia

***Ekwufulem ON,[1] Edema OT,[2] Iheji O,[3] Chukwukwe IO[1]**

ABSTRACT

Glaucoma is a group of diseases characterized by progressive optic neuropathy for which intraocular pressure (IOP) is a modifiable risk factor. Visual deterioration despite adequate IOP control has led to investigation of vascular risk factors. This study assessed the relationship between primary open angle glaucoma (POAG) and mean ocular perfusion pressure (MOPP) in patients with hypertension and those without hypertension. It was a hospital-based study which involved subjects who had hypertension and non-hypertensives. Both groups had blood pressure check, IOP check, gonioscopy and dilated fundoscopy +78D. MOPP was calculated for both groups. An interviewer- administered structured proforma was used to record data. Data was analyzed using the statistical software package SPSS, version 24. There were 112 cases and 112 controls. Of the cases, 64.7% were females, mean age was 54.03±10.18 years. Systolic blood pressure (SBP), Intraocular pressure (IOP) and systolic perfusion pressure (SPP) were significantly higher in the hypertensive group than in controls while MOPP and Diastolic perfusion pressure (DPP) were significantly lower in the hypertensive group. MOPP in the hypertensive group was significantly lower (47.10±6.79mmHg) than in the non-hypertensive group (48.99±4.08mmHg) with p=0.012. MOPP in glaucoma patients in the hypertensive group was found to be significantly lower (46.16±4.80mmHg) than those without glaucoma (53.22±6.17mmHg) with p=<0.0001. Binary logistic regression found MOPP to be a predictor of glaucoma in the hypertensive group (p=0.001 CL 0.703-0.909) unlike the controls. Prevalence of POAG in hypertensives was 12.5% and 2.7% for non-hypertensives. In conclusion, prevalence of POAG was significantly higher in hypertensives while MOPP was significantly lower in hypertensives.

Keywords: Open-angle glaucoma, hypertension, mean ocular perfusion pressure, intraocular pressure

INTRODUCTION

Glaucoma refers to a group of ocular diseases that have in common a characteristic optic neuropathy with associated visual field loss for which intraocular pressure (IOP) is one of the primary and modifiable risk factors.[1] Glaucoma is second only to cataract as a leading cause of global blindness and is a leading cause of irreversible visual loss.[2] The Nigerian National Blindness survey reported prevalence of blindness to be 4.2% (95% confidence interval 3.8-4.6%),16.7% of blindness being due to glaucoma in adults aged 40 years and above.[3]Primary open angle glaucoma (POAG) has been found to be more common and have a worse progression in Africans.[4]

Intraocular pressure is the only modifiable risk factor for glaucoma and the risk of glaucoma increases with raised intraocular pressure however, the relative contribution intraocular pressure makes to glaucoma risk appears to be small in some patients.[5] this has led to the investigation of vascular risk factors of glaucoma. Factors that affect the blood supply to the optic nerve head are thought to play a significant role in causing glaucomatous optic neuropathy and these factors are termed

Ophthalmology Department,[1] FMC Umuahia, Abia State, Nigeria.
Ophthalmology Department,[2] UBTH, Benin City, Edo State, Nigeria.
Cardiology Unit,[3] Department of internal medicine3, FMC, Umuahia, Abia State, Nigeria.

*Corresponding author:droluchilens@yahoo.com
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vascular risk factors.[6] Vascular risk factors that have been found to be capable of causing optic neuropathy include systemic hypertension, hypotension, ocular perfusion pressure, atherosclerosis and vasospasm.[7] Hypertension is defined as systolic blood pressure (SBP) of 140mmhg or more, and/or a diastolic pressure (DBP) of 90mmHg or more.[8] Hypertension has been found to be a worldwide epidemic. Approximately 20% of the world's adults have hypertension accounting for about 1 billion people.[9] There is a higher prevalence of hypertension in Africans.[10] In Nigerian studies, the overall prevalence of hypertension ranges from 8% to 64% depending on the target study population, type of measurement and cut off value used for its definition.[11]

Some population-based studies have reported an association between increase in blood pressure and increase in intraocular pressure.[12,13] Similarly, Orzalesi et al[14] in their study in Italy found primary open angle glaucoma to be significantly associated with hypertension. However, Pache and Flammer[15] suggested that hypotension play more role in causing optic neuropathy than systemic hypertension. They explained that nocturnal hypotension which occurs during sleep may be accounted for by sympathetic withdrawal during sleep.

Ocular perfusion pressure (OPP) is defined as the difference between mean arterial pressure (MAP) and venous pressure (VP)where the venous pressure is substituted with the intraocular pressure (IOP) since it is equal to or slightly greater than it.[16] It determines the amount of blood that gets to the optic nerve head resulting in either adequate perfusion or under-perfusion. It is calculated using a standard formula which assesses the relationship between blood pressure and intraocular pressure. When intraocular pressure rises enough to reduce the ocular perfusion pressure beyond the capacity for auto-regulation, ocular blood flow become reduced resulting in retinal dysfunction and optic neuropathy. While Kyari et al[17] demonstrated a lower ocular perfusion pressure in patients with primary open angle glaucoma, Omoti et al[18] reported a higher ocular perfusion pressure in glaucoma patients.

Having observed some progression in glaucoma patients who attend the eye clinic of Federal Medical Centre, Umuahia despite good intraocular pressure control as evidenced by deteriorating visual field, it became necessary to investigate vascular risk factors with emphasis on hypertension and ocular perfusion pressure. Systemic hypertension is very common in our environment and also there have been inconsistencies in results as regards relationship between it and primary open angle glaucoma in foreign and local studies. Furthermore, some inconsistencies exist in reports concerning ocular perfusion pressure even among African studies. In addition, paucity of data in our locality on the subject matter prompted the need to determine frequency of POAG and the MOPP in patients with hypertension and those without hypertension in Federal Medical Centre, Umuahia.

MATERIALS AND METHODS

A cross- sectional, case-control study was carried out at eye clinic and cardiology clinic of Federal Medical Centre, Umuahia, Abia State between June 2018 and November 2018. Ethical approval was obtained from the Ethical Committee of Federal Medical Centre, Umuahia Health Research and Ethics Committee. Systematic sampling technique was used to select patients for the study. Every third hypertensive patient who gave consent to the study and who met the inclusion criteria was recruited for the study in the case group. Similarly, every third new patient seen at the eye clinic who met the inclusion criteria was recruited for the control group until the required sample size was reached. They were age and sex matched with the cases and gave consent.

Inclusion Criteria for hypertensive patients

New patients who presented to the cardiology clinic and were diagnosed by the physician to have hypertension or old hypertensive patients on follow up visit to the cardiology clinic who were 40 years and above, within the study period. All eligible patients who gave consent.

All eligible patients whether on treatment or not.

Exclusion Criteria for hypertensive group

- Hypertensives who were on treatment for glaucoma.
- Previous ocular trauma or diseases.
- Hypertensive patients who were unable to complete the interview and examination process.

Inclusion criteria for control group

- Patients who did not have hypertension and who were not on anti-hypertensives.
- Patients who had not been diagnosed with glaucoma and were not on antiglaucoma drugs.
- Age and sex matched patients.
- Patients who gave consent.

Exclusion Criteria for Control Group

- Patients who were already diagnosed with hypertension or glaucoma.
- Non consenting patients or patients who failed to complete the examination process.

Sample Size Determination

The minimum sample size was determined using the formula for comparisons for populations less than 10,000[92]viz:

$$N=\frac{[A+B]^2 \times [(p1 \times (1-p1)) + (p2 \times (1-p2))]}{[p1-p2]}$$ [19]

Which gave an estimated value of 102.375 which was approximated to 112 allowing for an attrition rate of 10%. There were 112 cases and 112 controls.

Definition of hypertension: Systolic blood pressure (SBP) of 140mmHg or more, and/or a diastolic pressure (DBP) of 90mmHg or more.[8]

Criteria for diagnosis of primary open-angle glaucoma: Any 2 or more of the following[20,21]

Glaucomatous cupping (vertical cup-to-disc ratio of ≥0.5 or vertical cup disc ratio asymmetry ≥ 0.2), Central visual field suggestive of glaucoma (ranging from enlarged blind spot to tunnel vision) Open anterior chamber angles on gonioscopy (Shaffer grade3 or 4)
with or without raised intraocular pressure (> 21mmHg) at presentation.

Intraocular pressure*:* Elevated intraocular pressure was defined as >21mmHg.[20]
Mean arterial pressure (MAP): DBP+ 1/3 (SBP-DBP). [23]
(DBP= Diastolic blood pressure)
Calculating Mean ocular perfusion pressure: MOPP = 2/3 x [MAP-IOP]. [23]
Systolic perfusion pressure: Systolic blood pressure – Intraocular pressure mmHg [24]
Diastolic perfusion pressure: Diastolic blood pressure – Intraocular pressure mmHg[24]

Data was collected using self-prepared, interviewer-based proforma. Information collected included demographic data, medical history, medical examinations such as blood pressure, visual acuity, intraocular pressure, anterior segment examination findings and dilated fundoscopy findings. The blood pressure was measured by the principal investigator using a mercury sphygmomanometer with the patient in siting position. Two blood pressure measurements were taken, 5 minutes apart and the average taken as the final entry blood pressure. The intraocular pressure was taken by the principal investigator using a Perkins hand held applanation tonometer. Two readings were taken for each eye, 5 minutes apart and the average taken to be the patients' intraocular pressure. The anterior segment exam was

done using a pen torch initially and the slit lamp subsequently. The principal investigator also performed a dilated fundoscopy using a +78D lens together with a slit lamp biomicroscope. Subsequently, the MOPP was calculated using a standardized formula as stated above. This was done for both cases and control.

The data collected from the study was entered in excel spread sheet and analysed using statistical package for scientific solutions software (SPSS) version 24 software after the cleaning of data. Results were presented in tables and figures. Quantitative data was analysed using t- test while Chi- square or Fisher's exact test where an expected cell count was less than 5 were used to compare the qualitative variables. The relationship between mean ocular perfusion pressure and blood pressure was analysed using Pearson's correlation coefficient. Unadjusted and adjusted logistic regression was conducted at a 95% confidence interval to determine predictors of glaucoma among hypertensive patients in Federal Medical Centre, Umuahia.

RESULTS

224 subjects were examined, the hypertensive group consisted of 112subjects with 110 right eyes and 112 left eyes while the non-hypertensive group consisted of 112subjects with 112 right eyes and 112 left eyes. 2 subjects in the hypertensive group had right eye evisceration. Both groups were age and sex-matched and were subjects who met the inclusion criteria. The demographic characteristics of the subjects are shown in table 1. A greater percentage of the subjects were females (64.7%) with a male-to-female ratio of 1:1.8. The ages of the respondents were spread between 40-90 years, the mean age of the study's population was 54.03±10.18. The mean age of the hypertensive group [57.59±9.28] was higher than the non-hypertensive group [50.47±9.83]. Most of the respondents (58.0%) had tertiary education, 82.1% were married and 95.1% were Igbos (Table I).

For the purpose of this study, data from the left eyes was analysed since there was no significant difference in MOPP values between the right and left eyes (RE: 52.66±5.23, LE: 52.77±5.36, p=0.832).

The mean SBP, 1OP and SPP were significantly higher in the hypertensive group than non- hypertensive group while mean OPP and DPP were significantly lower in the hypertensive group than the non-hypertensive group. (Table 2)

The mean intraocular pressure in the hypertensive group was higher when compared to the non-hypertensive group. (Table 3)

The frequency of POAG in the hypertensive patients was 12.5% (14/112), while in the non-hypertensives the frequency was 2.7% (3/112), this difference was statistically significant with p=0.006. (Table 4).

Graph 1 shows that in the hypertensive group, the MOPP was significantly lower (p=0.0001) in patients with glaucoma when compared with non-glaucoma patients.

While table 5 shows unadjusted binomial logistic regression analysis on the predictors of glaucoma

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Table 1: Demographic Characteristics of the Study Participants

Variable	Non-hypertensive (N =112) %	Hypertensive (N=112%)	Frequency (N=224)	χ^2	P value
Gender					
Male	43(38.4%)	36(32.1%)	79 (35.3%)	0.958	0.328
Female	69(61.6%)	76(67.9%)	145 (64.7%)		
***Age**					
40-49	41(36.6%)	45(40.2%)	86 (38.4%)	1.324	0.542
50-59	39(34.8%)	42(37.5%)	81 (36.2%)		
60-69	20(17.9%)	15(13.4%)	35 (15.6%)		
70-79	9(8.0%)	10(8.9%)	19 (8.5%)		
80-89	2(1.8%)	0(0%)	2 (0.9%)		
≥90	1(0.9%)	0(0%)	1 (0.4%)		
Marital status					
Single	5 (4.5%)	4(3.6%)	9 (4.0%)	6.653	0.065†
Married	98(87.5%)	86(76.8%)	174 (82.1%)		
Divorced	0(0.0%)	1(0.9%)	1(0.4%)		
Widowed	9(8.0%)	21(18.8%)	30 (13.4%)		
Educational					
Status					
None	5(4.5%)	6(5.4%)	11(4.9%)	1.739	0.633†
Primary	6(5.4%)	10(8.9%)	16(7.1%)		
Secondary	32(28.6%)	35(52.2%)	67(29.9%)		
Tertiary	69(61.6%)	61(54.5%)	130 (58.0%)		

*****Mean age: 54.03±10.18 years (Inter Quartile Range: 46-60); Range 40-90 years. †Fishers' Exact test; ††Yates continuity correction

Table 2: Clinical Characteristics of the Study Participants

Variable (mean)	Non-hypertensive (N =112)	Hypertensive (N=112) *	t value	p-value
SBP	120.58 ±8.90	128.21 ±14.47	-4.756	0.0001*
DBP	77.38 ±7.27	76.52 ± 9.65	0.751	0.454
MAP	91.68 ±6.12	93.63 ± 10.04	-1.754	0.081
IOP	12.07 ±2.06	14.71 ± 3.36	-7.105	0.0001*
OPP	48.99 ± 4.08	47.10 ± 6.79	2.526	0.012*
SPP	108.52 ±9.00	113.16 ± 14.27	-2.91	0.004*
DPP	65.30 ±7.2	60.46 ± 12.61	3.526	0.001*
VCDR	0.31 ±0.08	0.38 ± 0.12	-4.772	0.0001

Abbreviations: DBP: diastolic blood pressure; SBP: systolic blood pressure; IOP: intraocular pressure; OPP: ocular perfusion pressure. SPP: Systolic perfusion pressure, DPP: Diastolic perfusion pressure, VCDR: Vertical cup disc ratio. *Significance <0.05

Table 3: Mean Intraocular Pressure of Study Participants

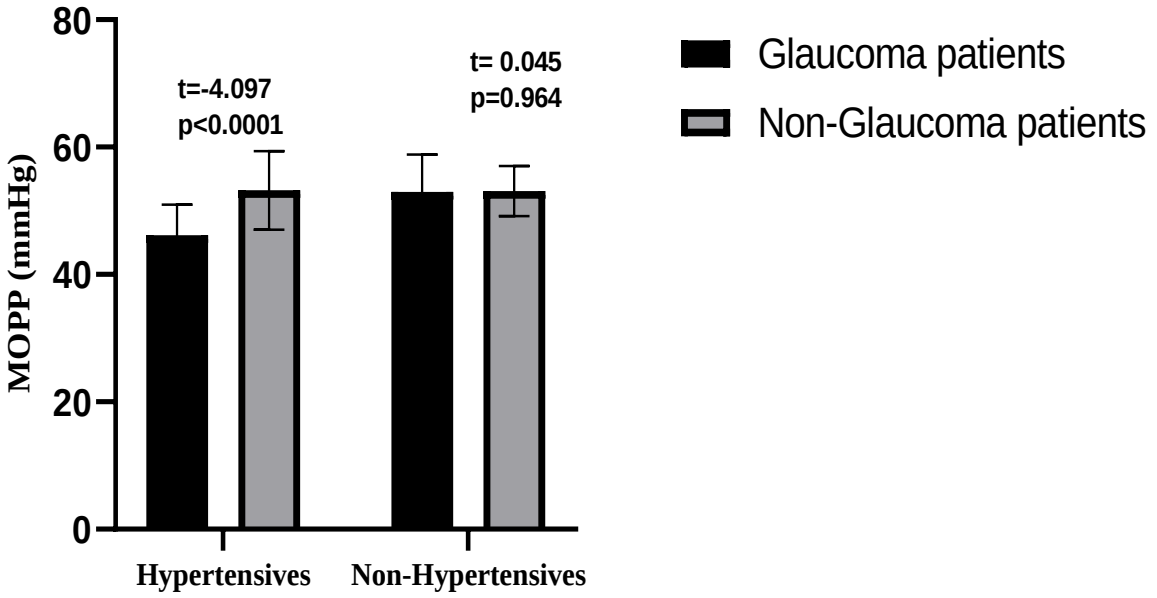
IOP	Non-hypertensives (n %)	Hypertensives (n%)	P value
<21mmHg	112 (100.0%)	106(94.6%)	0.039**
≥21mmHg	0 (0.0%)	6 (5.4%)	
Total	112 (100%)	112 (100%)	

**significance<0.05

Table 4: Distribution of Primary open-angle glaucoma among Hypertensives and non-Hypertensives

	HYPERTENSION (n=112)	NO HYPERTENSION (n=112)	χ^2	P value
Glaucoma	14 (12.5%)	3 (2.7%)	7.702	0.006*
No glaucoma	98 (87.5%)	109 (97.3%)		
Total	112 (100%)	112 (100%)		

*significance<0.05



Graph 1*:* Association between mean ocular perfusion pressure and primary open-angle glaucoma

Table 5: Unadjusted Binomial logistic regression analysis on the predictors of Glaucoma

.	Reference	B	df	OR	95% CI	P
Gender (Female)	Male	-0.532	1	0.587	0.217-1.588	0.294
Age	Unit increase	0.007	1	1.007	0.96-1.056	0.776
IOP(≥21mmHg)	IOP<21mmHg	4.024	1	55.909	10.098-309.556	<0.0001*
Hypertension	Non-hypertensive group	1.647	1	5.19	1.448-18.602	0.011*
SPP	Unit increase	-0.063	1	0.939	0.892-0.989	0.018*
DPP	Unit increase	-0.132	1	0.877	0.816-0.942	<0.0001*
SBP	Unit increase	-0.015	1	0.985	0.945-1.027	0.485
DBP	Unit increase	-0.055	1	0.946	0.889-1.008	0.088
MOPP	Unit increase	-0.231	1	0.794	0.709-0.890	<0.0001*

Using unadjusted binomial regression, patients with hypertension were 5 times (OR 5.17) more likely to have glaucoma. With a unit decrease in MOPP the patients were 1.3 times (1/0.794) more likely to have glaucoma, this was statistically significant with p=<0.0001.

DISCUSSION

The mean age of the study population was 54.03±10.18 years. This is similar to the mean age reported by Omoti et al[18] (55.9±18.3 years) in Benin City, Onakoya et al[20] (55.7±11.3years) in Lagos, Nigeria and Ihemedu (53.6±8.7 years) in Osun State.[25] This may be because hypertension and glaucoma are commoner in this age group and also that this age group is the working age group who are economically empowered to seek medical attention. The mean age of hypertensives was 57.59±9.28 years. This was similar to the mean age of hypertensives as seen in the study by Onakoya et al[20] (56.7 ± 12.95 years) in Lagos and Yadev et al[26] (54.9 ± 11.0 years) in India possibly because hypertension usually comes with increasing age. There were more females (64.7%) than males (35.3%). This is in contrast to the report by Omoti et al[18] who reported more males (62.11%) than females (37.89%). Environmental differences may account for this as males in the southeast are so engaged in business and so do not retire like civil servants do, therefore they may not readily leave their shops to seek medical attention. It is not surprising that 95.5% of the respondents were Ibos considering that the study was carried out in South East, Nigeria and 99.1% were Christians which is the commonest religion practiced in that part of the country.

The mean IOP was significantly (p=0.0001) higher in the hypertensive group (14.71±3.36mmHg) when compared to the non-hypertensive group (12.07±2.06mmHg). A similar relationship was also found between blood pressure and intraocular pressure in hospital based studies done in Nigeria by Omoti et al[18] and Onakoya et al.[20] This positive relationship between intraocular pressure and blood pressure was also found in population based studies such as the Rotterdam Study,[12] Blue Mountain Study,[27]Egna-Neumarkt Study,[28] and the Beaver Dam Eye Study.[29] The possible explanation for this increased IOP in the hypertensive group is that the mechanisms relating to change in sodium transport at receptors of the renal tubule epithelia in systemic hypertension also act in the ciliary epithelia in primary open angle glaucoma.[30] The systolic blood pressure was significantly higher in the hypertensive group (p=0.0001) when compared to the non- hypertensive group. This is similar to the findings from population-based studies by Hennis et al[31] Barbados Eye Study,[32] and the Latino Eye Study.[33] Increased systolic blood pressure was also found to be associated with increased intraocular pressure in studies done in Asia.[34,35]

In this study, 12.5% of the patients in the hypertensive group had POAG and 2.7% of the non-hypertensives had POAG (p=0.012). This is in agreement with findings of Onakoya et al[20] who reported 38.7% of hypertensive patients to have POAG and 18% of non-hypertensives to have POAG. Our findings are similar to findings of other studies done in Nigeria by Omoti et al[18,] and Agbeja et al.[36] Similar findings have been reported in population-based studies done outside Nigeria: the Baltimore Eye Survey[37] and Egna-Neumarkt study.[28] The possible explanation to this positive relationship between systemic hypertension and POAG may be the higher intraocular pressure found in the hypertensive group. The other possible explanation to it may be that long term increase in blood pressure may cause arteriolosclerosis with resultant increased resistance to blood flow and subsequent reduction in ocular perfusion pressure[38] considering that 64% of our study participants had had hypertension for over 1 year. Prolonged hypertension is associated with disruption in auto regulation resulting in reduced blood flow to the optic nerve head and subsequent reduction in its perfusion.[33] In this study it was observed in multivariate analysis that hypertension was a predictor of glaucoma, it was found that a patient who had hypertension was 5 times (OR 5.17 CI 1.448-18.602 mmHg) more likely to have POAG using unadjusted binomial regression. When adjusted

binomial regression was used, the likelihood of a hypertensive having POAG dropped to 3 times (OR 3.22 CI 0.585-17.729mmHg). However, it was no longer found to be statistically significant. Conversely, Leske et al reported that hypertension may offer protection against POAG. The explanation being that increased blood pressure may cause a temporary increase in perfusion to the optic nerve head. However, this protection may be lost in prolonged hypertension causing the patient to eventually come down with compromised perfusion to the optic nerve head resulting in glaucoma.

The MOPP in this study was statistically lower (p=0.012) in the hypertensive group (47.10±6.79mmHg) when compared to the non-hypertensive group (48.98±4.08mmHg). The MOPP in hypertensive patients who have glaucoma (46.16±4.80mmHg) was significantly lower (p=0.0001) than in hypertensive patients who did not have glaucoma (53.22±6.17mmHg). This association is similar to what was reported by the Early Manifest Glaucoma Study[39] and Rotterdam Study.[40] The Nigerian National Blindness and Visual Impairment Survey[17] reported MOPP to be a risk factor for POAG in Nigeria. Using unadjusted binomial logistic regression, MOPP was found to be a predictor of glaucoma (p=<0.0001 CI 0.709-0.890). However, adjusted binomial logistic regression did not show MOPP to be a predictor of glaucoma. This could be explained by the fact that a reduced perfusion pressure may cause a significant reduction in ocular blood flow especially if autoregulation is absent like in prolonged hypertension. In our study, a positive correlation was found between MOPP and SBP in both hypertensives (0.747) and non-hypertensives (0.610). A similar positive correlation was found between MOPP and diastolic blood pressure in non-hypertensives (0.790) and hypertensives (0.806). This correlation between MOPP and SBP/ DBP is more pronounced among the hypertensives and even among the hypertensives. DBP was more correlated with MOPP than SBP. It can be inferred that with a decrease in SBP and DBP, OPP will be decreased and that this effect will be more with a decrease in DBP which has a higher correlation with MOPP than SBP. MOPP which has been found to play a role in the development and progression of POAG in hypertensive patients is an important parameter in the evaluation of these hypertensive patients with glaucoma. Additionally, Blood pressure and intraocular pressure measurements are important in the determination of MOPP. MOPP that will ensure adequate optic nerve head perfusion is determined by a balance between blood pressure and intraocular pressure, therefore in hypertensives, these two parameters should not be viewed in isolation.

We therefore recommend that Ophthalmologists should determine MOPP for hypertensive patients with glaucoma so as to ensure that the optic nerve head is not further compromised by poor perfusion. More so, in hypertensive patients who have glaucoma, the blood pressure should be taken into consideration when setting target pressure to ensure adequate perfusion to the optic nerve. There is need for further studies on the optimal MOPP that will protect the optic nerve head from glaucomatous damage.

LIMITATIONS OF THE STUDY

The effect of circadian perfusion pressure fluctuation which is a known risk factor for glaucoma was not assessed since BP and IOP were measured during one hospital visit. Furthermore, all hypertensives were on treatment, so the blood pressures were modified and not true representation of the real blood pressure of hypertension.

CONCLUSION

The frequency of POAG is significantly higher in hypertensives compared to non-hypertensives furthermore, the MOPP was found to be significantly lower in the hypertensive group compared to the non-hypertensive group. Moreover,

among hypertensive patients, the mean ocular perfusion pressure was found to be significantly lower in glaucoma patients when compared to no-glaucoma patients. There may be a need to monitor hypertensives closely for the risk of POAG.

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CONFLICT OF INTEREST

We hereby declare that the study and manuscript submitted for publication are free of any form of interest and were fully funded by the authors.

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