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Ophthalmology

EVALUATION OF SYSTEMIC HYPERTENSION AS A RISK FACTOR FOR PRIMARY OPEN ANGLE GLAUCOMA

Dr Elizabeth Sunalini MS Ophthalmology, Senior Resident, Central Railway Hospital, Lallaguda, Telangana-500017, India.

ABSTRACT The main objectives of this study is to determine if systemic hypertension is a risk factor for developing primary open angle glaucoma (POAG) and to evaluate the role of mean Ocular Perfusion Pressure as a risk factor for primary open angle glaucoma (POAG).

KEYWORDS : IOP-Intraocular pressure, ONH- Optic nerve head ,POAG-Primary open angle Glaucoma,ACG-Angle closure glaucoma

INTRODUCTION

Glaucoma is the second most common cause of blindness worldwide[1]. It is a major global issue,causing significant ocular morbidity and disability due to its progressive nature resulting in an irreversible visual loss[2]. Patients are usually asymptomatic until very advanced stage,making visual loss irreversible by the time they present to an ophthalmologist[3,4].One of its variant and most common form-primary open angle glaucoma(POAG) is a chronic, progressive and anterior optic neuropathy that is associated with characteristic cupping and atrophy of the optic disc,visual field loss,open angles,and no obvious causative ocular or systemic conditions[5]. POAG accounts for nearly three-quarters(74%) of all glaucoma cases[6,7]. Various estimates and meta-analysis data show that estimated there could be 60,500,000 people with open-angle glaucoma(OAG) and angle-closure glaucoma(ACG) in 2010[6,9]. With an expected increase in population and longevity, Primary Open Angle Glaucoma(POAG) is likely to become a major cause of ocular morbidity in the developing world over the next few years Primary Open Angle Glaucoma(POAG) is multifactorial optic neuropathy in which there are characteristic atrophic changes of optic nerve with associated visual field defects[6]. Worldwide, the reported prevalence for primary open-angle glaucoma varies between 1.62% and 3.51%[8].

MATERIALS AND METHODS

STUDY TYPE-Hospital based retrospective type of Case-Control STUDY performed at out patient department(OPD) and wards of Department of ophthalmology of south central railway, Secunderabad.

SAMPLE SIZE-by applying the equation for calculating sample size for correction type of cross-sectional, case control study in the outpatient department (OPD) and wards of department of ophthalmology.

DURATION of STUDY- July 2018 to June 2020

SAMPLE SIZE- it is determined by using formula,

$N=(z)^2pq/d^2$

N=Sample size estimate
Z=Standardized normal deviate(1.96)
p=Proportion of target population with characteristic being measured
q=100-p
d=relative precision

Based on the "Blue Mountains eye study" prevalence is taken as (p)=65%.Relative precision set to be 10%.So "d" is 10% of "p" d=6.5

So in our study N=(1.96*1.96)*65*35/6.5*6.5
N=206
Roughly "N" is taken as 200. So N=200

ELIGIBILITY CRITERIA:

INCLUSION CRITERIA-

*Age >40 yrs of age
*Patients attending OPD with Primary Open Angle Glaucoma as cases
*Age and Sex matched controls without Primary Open Angle Glaucoma as cases in the ratio of 1:1.

EXCLUSION CRITERIA-

*Recent ocular surgery done for causes other than glaucoma and
*Grade 4 cataract or Mature cataract patients
*Patients <40 yrs of age
*Secondary glaucoma
*Uveitis
*Corneal scarring or opacity which would hamper evaluation of post.segment
*Other causes of optic atrophy
*Congenital Glaucoma.
*Patients with Diabetes Mellitus
*Patients with Family History of Glaucoma
*Patients with Diabetes,Hyperlipidemia,Myopia,Migrane

METHOD OF COLLECTION OF DATA:

Patients with a diagnosis of Primary open angle Glaucoma presenting to the department of Ophthalmology were included in the study along with age and sex matched non- hypertensive controls. Informed consent was taken from all patients prior to inclusion in the study. A detailed history of past medical illness including Systemic hypertension, ocular disease history taken. History of any medications that the patient was on was also included.

Hypertension was defined as a past history of hypertension currently receiving antihypertensive treatment, or a systolic BP >140 mmHg and/or a diastolic BP >90 mm Hg at the time of examination as per the Joint National Committee (JNC) 7 guidelines.[7]

A detailed physical examination and ophthalmological examination was done.

Blood pressure was recorded with the patient in sitting position after resting for five minutes. Patients were classified as hypertensives as per JNC 7 guidelines, or if the patient was a known case of hypertension on antihypertensive medications.

OPHTHALMOLOGICAL EXAMINATION -

Best corrected visual acuity (BCVA) was assessed using an illuminated Snellen's chart, with the patient seated at 6 meters distance. Near vision was assessed, using Jaeger's near vision chart.

Colour vision was checked using Ishihara's pseudo-isochromatic charts.

Slit lamp examination was performed to rule out anterior segment pathology.

Gonioscopy was done with Goldmann's single mirror goniolens and the anterior chamber angle was graded according to Modified Shaffer's grading. Only patients with open anterior chamber angles were included in this study.

Dilated fundus examination by indirect ophthalmoscopy, followed by a slit lamp biomicroscopic evaluation with 78 D lens to evaluate the posterior pole including the optic disc was done.

Intraocular pressure (IOP) was measured using Goldmann applanation Tonometer. The IOP was measured three times in each eye, with the median value chosen as the intraocular pressure in that eye. IOP for a

person was defined as the highest of the pressures between the two eyes.

Central corneal thickness was measured using Pachymeter SP 3000 (Tomey Corporation) and this was used to calculate the corrected IOP for each eye of the patient.

The systolic blood pressure (SBP) and the Diastolic Blood pressure (DPP) recorded,Mean arterial pressure(MAP) were calculated .

Mean Ocular Perfusion Presure (OPP) calculated.
Mean OPP= 2/3 MAP - IOP
Visual field was tested using the Humphrey field analyzer, Zeiss model 720.

The test algorithm used was SITA standard 30-2. The visual fields were per the Anderrson Patella criteria and the severity of the glaucomatous field changes were graded according to the Hodapp, Parrish and Andersson classification guidelines given in the European Glaucoma Society guidelines for Glaucoma, 3rd Edition.

POAG was defined as patients with the following features; IOP >21 mmHg, cup:disc ratio > 0.4, and visual field changes suggestive of glaucoma.

Patients were divided into two groups:
Group 1: with POAG as Cases and
Group 2: without POAG as Controls for the purpose of analyzing the Hypertension as risk factor . For some parameters such as C:D ratio, IOP, central corneal thickness and diastolic perfusion pressure, each eye was analyzed separately as there could be differences between the two eyes of the same patient which would be missed if both eyes were evaluated together.

DISCUSSION

The results of the study showed that patients with Systemic Hypertension having risk of Developing Primary Open angle Glaucoma is(POAG) **1.991** times higher than Normotensive People.

Mean Ocular Perfusion Pressure is found to be lower in Patients with Hypertension patients Than Normo-tensive patients ,which leads to reduced blood circulation of Optic Nerve Head In Hypertensive patients.

Age appears to be an independent risk factor for development of primary open angle glaucoma (POAG). However, this was lower in our study with the mean(+ SD) age of patients being **55.86 ± 6.493 yrs,** and the mean (+SD) in patients with primary open angle glaucoma (POAG) being 57.73 ± 5.93 . Findings similar to our study were noted in The Aravind Comprehensive Eye Survey [8], where the median age of those with glaucoma was found to be 60.0 years (range 40–85 years; mean, 60.8 years). These findings suggest that primary open angle glaucoma (POAG) may be occurring in a younger population in the Indian subcontinent.

We found increasing age to have a statistically significant correlation (p=0.035) to the increased occurrence of primary open angle glaucoma (POAG). This was similar to the findings in the blue mountain eye study[11], the study by Leske et al , and in India in the study by Vijaya et al. Even the Baltimore eye survey found that the prevalence of glaucoma increases with age particularly among darker skinned races, exceeding 11 % in those aged 80 years or older .

In our study it showed that Systemic Hypertension is a statistically significant correlation with the occurrence of primary open angle glaucoma (POAG) (**p = 0.016*) .Odds Ratio = 1.991 (95% CI 1.133 to 3.497)** which is in concurrence with findings from the Blue Mountain eye study [11], Egna- Neumarkt study, Baltimore eye study, and the Rotterdam eye study . This was in contradiction to some population based studies such as the Barbados eye study, Chennai glaucoma study, the study by Weih et al , and the Aravind eye survey[8].

The study by **Topouzis et al**. found that both treated HTN (with BP within normal limits), and high systolic or diastolic BP are risk factors for POAG, with an OR for the presence of POAG being 2.04 (95% CI: 0.88–4.73) and 1.43 (95% CI 0.70–2.91), respectively . Moreover, the severity of glaucoma was found to be higher in patients with HTN than in glaucomatous individuals with a normal BP. The associations of SBP and DBP with glaucomatous optic neuropathy depend on the specifics of the patients studied—age, ethnic origin, concurrent diseases, other risk factors, treatment of HTN, type of medication used, and vascular endothelial function. Several mechanisms have been suggested to explain the risk of the developing POAG in individuals with HTN. Abnormal neuro-metabolic-endothelial mechanisms of the vascular tone control in glaucoma patients is related to the effects of vasoactive factors—endothelin–1 (ET-1), neuropeptide Y (NPY), nitric oxide (NO), prostacyclin (PGI 2), tumor necrosis factor (TNF-alpha), cyclooxygenase (COX-2), and metalloproteinases (MMP-9). Variation in the levels of these factors leads to endothelial dysfunction and to dysregulation of the autonomic nervous system.Theoretically, the duration of HTN and degree of vascular damage could be correlated with the risk of glaucoma; however, none of the studies analyzed such an association. A study by Jung et al. found that glaucomatous patients with multiple retinal nerve fiber layer (RNFL) defects had a higher prevalenceof concomitant vascular diseases (including HTN, end-stage renal disease or cerebrovascular disease) compared to those with glaucoma and no RNFL defects . Additionally, HTN was found to be a risk factor for reduced RNFL in healthy individuals in the European Eye Epidemiology study . These results highlight the potential role of vascular insuciency, not only as a risk factor of glaucoma, but also for potential glaucomatous damage.

Increased Intra ocular Pressure (IOP) with age has been observed in many populations and may account in part for the relationship between age and glaucoma. The Egna-Neumarkt study showed Intra ocular Pressure (IOP) to increase significantly with age (p =0.001) but in our study increasing age was not associated with higher mean Intra ocular Pressure(IOP).

POAG was diagnosed in 64 out of 112 males and in 52 out of 88 females in this study; this difference was statistically significant (p=**0.023***). This was contrary to other studies such as the Aravind Comprehensive eye survey[8] and the study done by Leske et al in Barbados which showed that males were more likely to have primary open angle glaucoma (POAG).

Population based studies done in rural and urban south India, and in Central India also did not show any significant gender variation between patients with and without primary open angle glaucoma (POAG). The blue mountain eye disease study showed a higher incidence of primary open angle glaucoma (POAG) in women than in men[11], and similar findings were seen in the **Andhra Pradesh eye disease study**[10], where the odds of females having primary open angle glaucoma (POAG) was 1.3 (95% CI, 0.7, 2.6), although this was not statistically significant .

The association of systemic hypertension and primary open angle glaucoma(POAG) has been unclear for many years. Rational biological hypotheses have been proposed which predict that systemic hypertension could have both a harmful and a protective effect on the survival of retinal ganglion cells. Although these hypotheses provide a conceptual framework for understanding the potential association between optic nerve head perfusion and glaucomatous damage, very little epidemiological evidence has been able to support these ideas.

In the **Blue mountain eye study** [11] , hypertensive subjects had a 50% higher risk of glaucoma than normotensive subjects, independent of Intra ocular Pressure (IOP) and other risk factors. **The Rotterdam Study** also documented significant associations between POAG and hypertension. **The Egna-Neumarkt study** howesd a weak tendency toward an association between POAG and systemic hypertension, similar to findings in the Baltimore eye survey which reported non-significant increased odds for the relationship between hypertension and primary open angle glaucoma (POAG).

Our study correlation between Mean Ocular Perfusion Pressure and the occurrence of open angle glaucoma, which was similar to the findings in the Baltimore Eye Survey[47], the Egna-Neumarkt Study and Proyecto VER study.

Mean ocular perfusion pressure showed in our study in primary open angle glaucoma (POAG) patients Was **45.76 ± 5.93 mmhg** and among non-glaucoma subjects was **51.27 ± 5.52 mmhg**.With statistical significance of p value**(p=0.001).** Compared with same study conducted by Rekha Khandelwal, Rachit Khandelwal1 , Dhananjay Raje2 ,Deepa Kumar1, Anand et all showed 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.

Mean Ocular perfusion pressure found lower in POAG patients in our study compared to lower studies.

RESULTS

In our study titled '**Evaluation of Systemic Hypertension as a Risk Factor for Primary Open Angle Glaucoma**', 100 Primary Open Angle Glaucoma patients as Cases and 100 normal Patients with age and gender matched controls who presented to the department of Ophthalmology with various complaints were included.

STATISTICALANALYSIS:

Data was entered into Microsoft excel data sheet and was analyzed using SPSS 22 version software. Categorical data was represented in the form of Frequencies and proportions. **Chi-square test** was used as test of significance for qualitative data. Continuous data was represented as mean and standard deviation. **Independent t test** was used as test of significance to identify the mean difference between two quantitative variables.

Graphical representation of data:

MS Excel and MS word was used to obtain various types of graphs such as bar diagram.

p value (Probability that the result is true) of <0.05 was considered as statistically significant after assuming all the rules of statistical tests.

Statistical software:

MS Excel**,** SPSS version 22 **(**IBM SPSS Statistics, Somers NY, USA) was used to analyze data.

RESULTS:

Table 1: Mean Age Comparison among two Groups

	Group						P Value
	Glaucoma Present		Glaucoma Present		Total		
	Mean	SD	Mean	SD	Mean	SD	
Age	57.73	5.93	55.86	6.493	56.80	6.27	0.035*

Mean age of subjects with Glaucoma was 57.73 ± 5.93 years and among subjects without Glaucoma was 55.86 ± 6.493 years. There was significant difference in mean age between two groups.

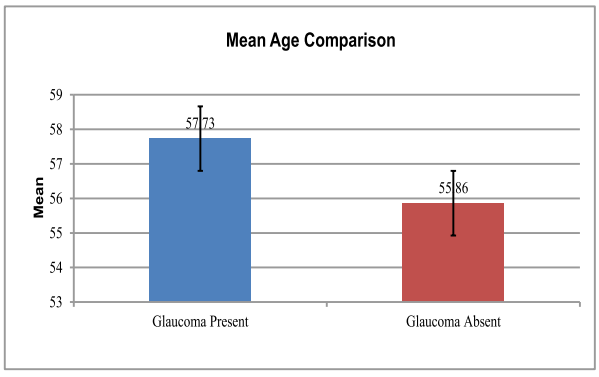

Figure 1: Bar Diagram Showing Mean Age Comparison among two Groups

Table 2: Age Distribution among two Groups

		Group					
		Glaucoma Present		Glaucoma Absent		Total	
		Count	%	Count	%	Count	%
Age	40 - 50 Years	17	17.0%	27	27.0%	44	22.0%
	51 - 60 Years	46	46.0%	46	46.0%	92	46.0%
	> 60 Years	37	37.0%	27	27.0%	64	32.0%

$\chi 2 = 3.835$, df = 2, p = 0.147

In the study in both groups, majority were in the age group 51 - 60 Years (46% respectively). There was no significant difference in age classification between two groups.

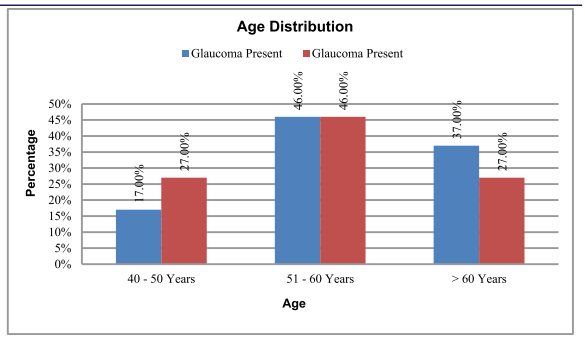

Figure 2: Bar Diagram Showing Age Distribution among two Groups

Table 3: Gender distribution between two groups

		Group					
		Glaucoma Present		Glaucoma Absent		Total	
		Count	%	Count	%	Count	%
Gender	Female	36	36.0%	52	52.0%	88	44.0%
	Male	64	64.0%	48	48.0%	112	56.0%

$\chi 2 = 5.195$, df = 1, p = 0.023*

OR = 1.96 (95% CI 1.093 to 3.393)

In the study among Glaucoma subjects, 64% were males and 36% were females and in Non-Glaucoma subjects, 52% were females and 48% were males. Hence Glaucoma was more among males compared to females. There was significant association between Glaucoma and gender.

Odds ratio was 1.96 I,e. males had 1.96 times higher risk of Glaucoma compared to Females.

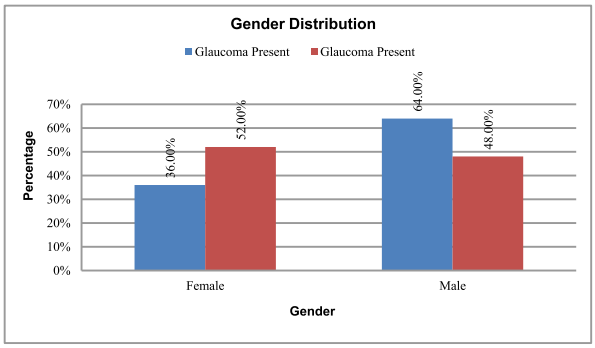

Figure 3: Bar diagram showing Gender distribution between two groups

Table 4: Mean SBP Comparison b/w two Groups

	Group						P Value
	Glaucoma Present		Glaucoma Absent		Total		
	Mean	SD	Mean	SD	Mean	SD	
SBP mm HG	136.61	9.835	133.76	10.473	135.18	10.23	0.049*

Mean SBP among Glaucoma subjects was 136.61 ± 9.835 mmhg and among non-glaucoma subjects was 133.76 ± 10.473 mmhg. There was significant difference in mean SBP between two groups.

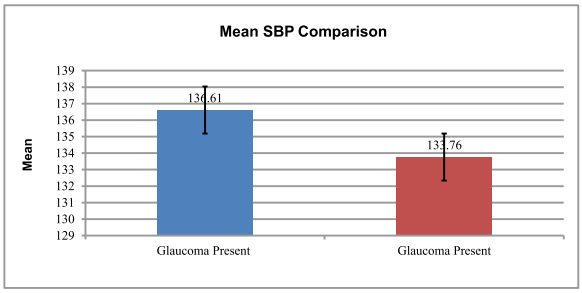

Figure 4 : Bar Diagram Showing Mean SBP mm HG Comparison among two Groups

Table 5: Mean DBP Comparison b/w two Groups

	Group						P Value
	Glaucoma Present		Glaucoma Absent		Total		
	Mean	SD	Mean	SD	Mean	SD	
DBP mm HG	85.38	8.04	83.13	7.60	84.26	7.89	0.043*

Mean DBP among Glaucoma subjects was 85.38 ± 8.04 mmhg and among non-glaucoma subjects was 83.13 ± 7.60 mmhg. There was significant difference in mean DBP between two groups.

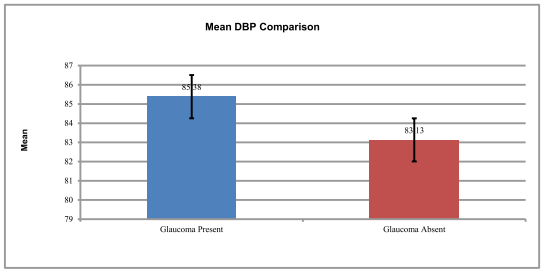

Figure 5: Bar Diagram Showing Mean DBP Comparison among two Groups

Table 6: Mean MAP Comparison among two Groups

	Group						P Value
	Glaucoma Present		Glaucoma Absent		Total		
	Mean	SD	Mean	SD	Mean	SD	
MAP	102.46	8.36	100.01	8.22	101.23	8.36	0.038*

Mean MAP among Glaucoma subjects was 102.46 ± 8.36 mmhg and among non-glaucoma subjects was 100.01 ± 8.22 mmhg. There was significant difference in mean MAP between two groups.

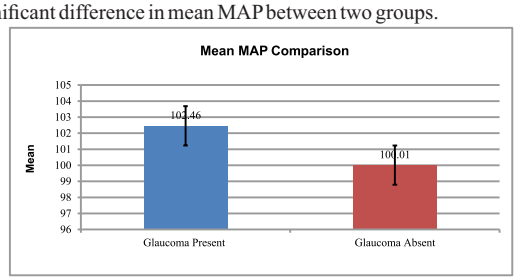

Figure 6 : Bar Diagram Showing Mean MAP Comparison among two Groups

Table 7: Mean Right and Left Eye IOP Comparison among two Groups

	Group						P Value
	Glaucoma Present		Glaucoma Absent		Total		
	Mean	SD	Mean	SD	Mean	SD	
Right Eye IOP	22.89	1.70	15.73	2.45	19.31	4.16	< 0.001*
Left Eye IOP	21.68	1.74	15.73	2.45	18.71	3.66	< 0.001*

Mean IOP of Right eye among Glaucoma subjects was 22.89 ± 1.70 mmhg and among non-glaucoma subjects was 15.73 ± 2.45 mmhg. There was significant difference in mean IOP on right side between two groups.

Mean IOP of Left eye among Glaucoma subjects was 21.68 ± 1.74 mmhg and among non-glaucoma subjects was 15.73 ± 2.45 mmhg. There was significant difference in mean IOP on Left side between two groups.

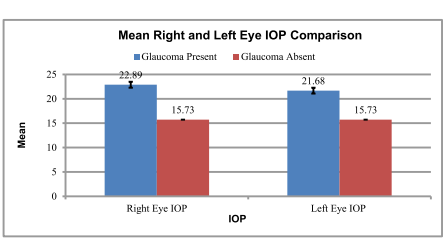

Figure 7: Bar Diagram Showing Mean Right and Left Eye IOP Comparison among two Groups

CONCLUSION

Primary open angle glaucoma (POAG) is a multifactorial disease and has various risk factors. It has an ambiguous relation to systemic hypertension and this has been evaluated in this study. Systemic hypertension was found to have a significant risk of development of primary open angle glaucoma (POAG) . Significant association was found between systemic hypertension and increasing Intra Ocular Pressure(IOP). These findings were different from those shown in many of the other population based studies done in other countries but were similar to the findings seen in studies done in India.

Lower mean Ocular perfusion pressure was also found to be significantly associated with primary open angle glaucoma (POAG) in this study.These findings were similar to other population based studies results.

Increasing age was found to be the most significant risk factor for primary open angle glaucoma (POAG) in this group of patients.

Nuclear sclerosis upto Grade 2 ,wont possess any risk of developing primary open angle glaucoma(POAG).

The differences in our findings as compared to other major studies could be attributable to the cross sectional study design, and institutional setting while most other studies have been prospective population based studies.

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