

STUDY OF RISK FACTORS IN PRIMARY OPEN ANGLE GLAUCOMA

Y. B. Bajantri¹, Rajashekar D.², Madhuri Parande³, Hemalatha A.⁴, Sneha Hegde⁵

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ABSTRACT: BACKGROUND: Glaucoma is one of the important causes of irreversible preventable blindness which is largely preventable if diagnosis is made before irreparable damage to vision has occurred. Understanding the risk factors, early diagnosis and prompt treatment could save useful vision in glaucoma patients. **OBJECTIVES:** To determine the risk factors associated with primary open angle glaucoma. **METHODS:** This is a hospital based descriptive study done at Department of Ophthalmology, Karnataka Institute of Medical Sciences, Hubli. 43 patients diagnosed with primary open angle glaucoma were enrolled into the study. Various risk factors of glaucoma were noted based on history and examination and data was compiled to obtain results. **RESULTS:** A total of 62 glaucomatous eyes of 43 patients were taken into analysis. Majority of patients (26; 60.46%) belonged to 51-70 age group. 95.35% were ≥ 40 yrs of age, 30.23% had diabetes, 27.91% hypertensive, 6.98% had family history, 11.63% were smokers and 2.32% were myopics. Mean IOP was 25.87 ± 8.4 mmHg. Majority of eyes (28; 45.16%) had IOP of 21-30 mmHg. **INTERPRETATION AND CONCLUSION:** Glaucoma related blindness is largely preventable through timely diagnosis, effective treatment and ongoing monitoring. Timely diagnosis - the first step - requires in depth knowledge of demographical aspects of glaucoma, namely the risk factors.

KEYWORDS: Primary Open Angle Glaucoma, Risk Factor, Intra Ocular Pressure.

INTRODUCTION: Glaucoma is the second leading cause of blindness in the world. It has been estimated that 80 million people worldwide will have glaucoma by the year 2020, of which 11.2 million will be blind.¹

Primary open angle glaucoma is a chronic, bilateral and often asymmetrical disease in adults in whom acquired loss of optic nerve fibres and abnormality in the visual field occur with an open anterior chamber angle of normal appearance and an intraocular pressure (IOP) which is detrimental to the structural and functional integrity of the optic nerve head.² Other synonymous terms that may also appear in the literature include chronic simple glaucoma (CSG), chronic open-angle glaucoma (COAG), and idiopathic open-angle glaucoma.

Population based studies show that a large portion of glaucoma remains undiagnosed. 50% of the affected are not even aware of it.² That so many with a potentially blinding and treatable condition are unaware about having the disease underscores the need for better screening strategies to identify those with glaucoma and bring them into care.

Risk factors are clinically useful to assess the risk for glaucoma based on the characteristics of the individual patient. Most of the evidence for chronic open angle glaucoma has been obtained from prevalence surveys or case-control studies.³ Age, race, increased IOP, a positive family history are considered significant risk factors in the development of glaucoma.

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AIM OF THE STUDY: The need of the hour is to detect and diagnose glaucoma at the earliest. Understanding the risk factors, early diagnosis and prompt treatment could save useful vision in glaucoma patients.

Risk factors for primary open angle glaucoma general risk factors:

Age: Population-based studies of prevalence and incidence consistently show a steady increase with age. As a rule of thumb, prevalence tends to roughly double for each decade over 40 (i.e., relative risk of 2 per decade) and is about 10-fold higher in the 80+ group compared to the 40 to 49 year-old group.

In the Early Manifest Glaucoma Trial (EMGT), the relative risk of progression of early glaucoma was 1.5 for those 68 years of age and older compared to younger persons.⁴

Family History: A family history of POAG is generally considered to be an important risk factor for POAG. Having a first-degree relative (parent, sibling, or child) with glaucoma has been consistently associated with an increased risk of POAG in prevalence surveys.^{5,6}

The odds ratio (OR) of POAG for a family history of glaucoma are higher if based on patients with previously diagnosed glaucoma (Baltimore OR = 4.7 Blue Mountain Eye Study OR = 4.2) than if based on newly detected cases (Baltimore OR = 2.8; Blue Mountain Eye Study OR = 2.4). This suggests that having a diagnosis of POAG leads to a greater awareness of glaucoma in the family. The association between POAG and family history may be stronger when the affected relative is a sibling (OR = 3.7) rather than a parent (OR = 2.2) or child (OR = 1.1).⁷ A population-based prospective study by Le A, et al showed Family history as a risk factor for glaucoma (Risk Ratio; RR = 2.1).⁸ while in the clinically assembled OHTS population no association was found.

Ocular Risk Factors: Intraocular Pressure: The evidence that IOP is a risk factor for glaucoma has recently become so strong that, unlike any other risk factor for glaucoma, it satisfies criteria.^{9,10} commonly used to assess causality.

There is a strong dose-response relationship between IOP and glaucoma that has consistently been shown in prevalence surveys and in longitudinal studies of incidence.^{8,11} and progression.¹²

The most decisive new evidence to be published in recent years was the demonstration by randomized clinical trials that IOP lowering decreased the incidence¹⁹ and progression of glaucoma.^{13,14} compared to no treatment.

In short, IOP is best considered both a risk factor and a cause of glaucoma. In the Baltimore Eye Survey, the prevalence of COAG increased with intraocular pressure. The prevalence of COAG in persons with an IOP of 35mmHg or greater was more than 40 times as high as that in persons with IOP of 15 mm Hg¹⁷

In the Barbados Eye Study, the incidence of COAG was found to increase steadily with IOP with a relative risk of 25 for an IOP of more than 25 compared to a reference group with an IOP less than.^{15,16}

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In COAG, the EMGT and the CNTGS have shown that an IOP reduction of 25% and greater than 30% cut the risk of progression by 33% and 50%, respectively, compared to no treatment.^{13,14}

The AGIS study that found that those with the greatest IOP reduction (Group A: mean IOP = 12.3 mm Hg on treatment vs. 23.3 mm Hg before treatment) had stable fields (based on mean field defect score; risk of progression in group was 14.4%) in contrast to groups with higher levels of IOP that showed progressive field loss over the 8-year follow-up period.¹² This suggests that, at least in hypertensive COAG, an IOP level exists below which progression of glaucoma is stopped or at least suppressed to sub clinical levels in most patients.

Optic Nerve Head: Numerous studies have reported an increased incidence of glaucomatous visual field defects among those with larger Cup: Disc ratios (CDR).¹⁷ The OHTS showed a 1.4-fold increase in the incidence of COAG among ocular hypertensive patients for every 0.1-unit increase in the baseline CDR.¹⁸

Optic disc haemorrhages were first recognized as a precursor to glaucomatous optic nerve damage by Bjerrum in 1889. In 1977, Drance provided the first longitudinal findings¹⁹, that, eyes with a disc haemorrhage had a higher risk of field progression. This was subsequently confirmed by others.²⁰

Myopia: Numerous clinic-based studies show an association between myopia and POAG, and population-based studies in different ethnic groups found rates of open-angle glaucoma 2–4 times higher for myopes.^{21,22} The risk of glaucoma appears greatest in persons with higher degrees of myopia.^{23,24} The Blue Mountains Eye Study reported 2-3 times increase in prevalence of glaucoma in individuals with myopia.²⁵

Systemic Risk Factors for POAG: Diabetes Mellitus: Population-based studies fail to consistently show an association between diabetes and POAG, although two studies on Hispanics and Whites in the United States showed a weak association between the two conditions.^{23,26,27,28}

Considerable controversy exists in literature regarding association between Diabetes Mellitus (DM) and POAG. The prevalence of POAG appears to be higher in the diabetic population by a factor of 2 in majority of population based surveys. A prevalence of 3.11 in Rotterdam study.²³ 1.84 in the Beaver Dam Eye Study.²⁶ and 2.12 in the Blue Mountain Eye Study.²⁷ has been reported.

IOP is important confounder of the association between diabetes and glaucoma because persons with diabetes appear to have slightly higher IOP and have been reported to have a higher prevalence of ocular hypertension compared to non- diabetics.^{3,22,28} Diabetes has not yet been shown to increase the incidence of glaucoma, it is probably a risk factor for glaucoma.³

HYPERTENSION: Higher systolic and diastolic blood pressures are associated with increased IOP.^{22,24}

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In the Baltimore eye study, IOP was 1.5 mmHg higher for patients with a systolic blood pressure over 160 mmHg when compared to systolic blood pressures lower than 110 mmHg.²⁴ The same study, however, did not find a statistically significant association between hypertension and glaucoma.

Likewise, no association was seen between POAG and hypertension in the Aravind Comprehensive Eye Study.²¹ among South Indians or Southwest United States Hispanics in a study conducted by Quigley et al.²⁴

In the Blue Mountain eye study, Hypertension was significantly associated with OAG, after adjustment for OAG risk factors including IOP, odds ratio (OR) 1.56, 95% confidence interval (CI:1.01-2.40). They concluded that Hypertension, particularly if poorly controlled, appears related to a modest, increased risk of OAG, independent of the effect of blood pressure on IOP and other glaucoma risk factors.

Cigarette Smoking and Alcohol Use: Some clinic-based studies suggest an association between alcohol consumption and glaucoma. However, no differences in the prevalence of glaucoma were noted with mild, moderate, or heavy alcohol consumption in the Beaver Dam Eye Study.²⁶

A small increase in IOP was noted in smokers in the Australia Blue Mountain Eye Study even after adjusting for numerous other variables.²⁷

The prevalence of POAG has not been observed to vary between smokers and non-smokers in other studies.^{24,26}

METHODOLOGY: MATERIALS AND METHODS: 43 patients of primary open angle glaucoma attending the ophthalmic outpatient department of Karnataka Institute of Medical Sciences during December 2012 to May 2014 were enrolled into the study after valid consent. Patients with angle closure glaucoma, secondary glaucoma and those with cataract were excluded from the study.

Demographic data of all patients are noted. Relevant history regarding ocular symptoms, family history of glaucoma, diabetes mellitus, hypertension, prior ocular surgery, and long term medication was taken.

Patient was subjected to the following examinations:

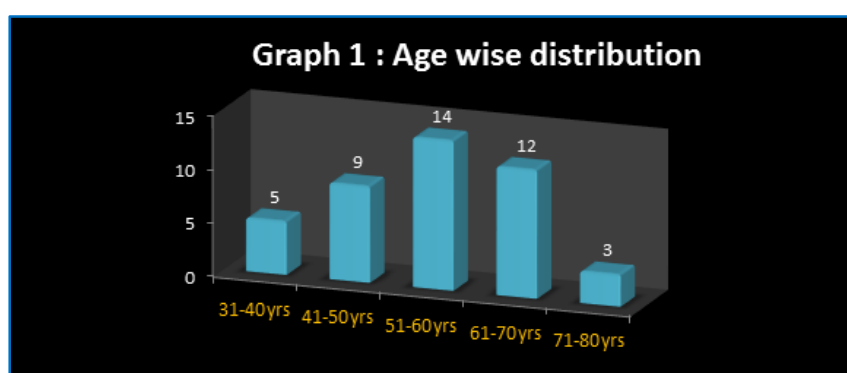
1. Visual acuity testing by Snellen's chart and best corrected visual acuity was recorded.
2. Slit lamp examination.
3. Intraocular pressure by Goldman's Applanation Tonometry (GAT).
4. Gonioscopy by Goldman's three mirror lens.
5. Direct Ophthalmoscopy, 90D lens examination, Indirect Ophthalmoscopy (IDO) to document optic disc status & to rule out other retinal lesions. Data was compiled and results were obtained.

RESULTS: Majority of patients (26) belonged to 51-70 age group; 14 (32.56%) in 51-60 and 12 (27.90%) in 61-70. Mean age was 55.95±11.

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Age groups	No. of patients	% of patients
31-40yrs	5	11.63
41-50yrs	9	20.93
51-60yrs	14	32.56
61-70yrs	12	27.90
71-80yrs	3	6.98
Total	43	100.00
Mean age	55.95	

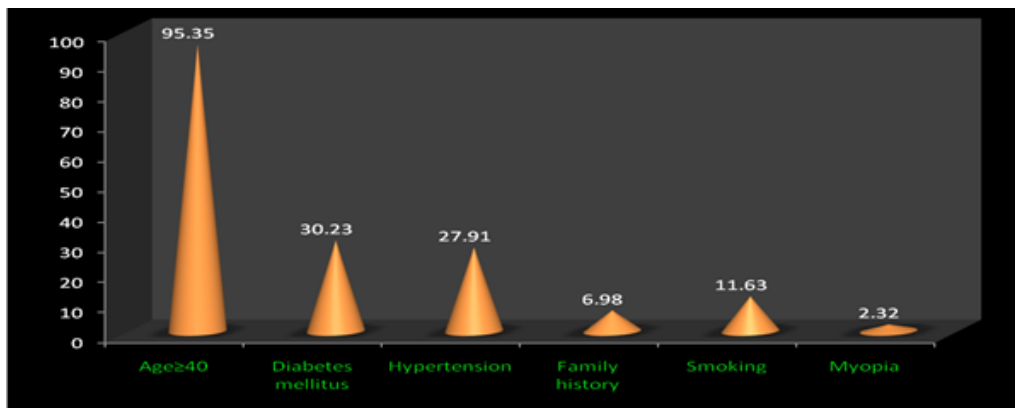
Table 1: Age wise distribution of patients



29 subjects (67.44%) were males. 41 patients (95.35%) were ≥ 40 yrs. of age; only 2 were < 40 yrs. old. 13 patients (30.23%) were diabetic and 12 (27.91%) had hypertension. 3 patients (6.98%) had family history of glaucoma. There were 5 smokers (11.63%) and 1 (2.32%) myopic in the study.

Risk factors	Present	%	Absent	%
Age ≥ 40	41	95.35	2	4.65
Diabetes mellitus	13	30.23	30	69.77
Hypertension	12	27.91	31	72.09
Family history	3	6.98	40	93.02
Smoking	5	11.63	38	88.37
Myopia	1	2.32	42	97.68

Table 2: Presence of risk factors



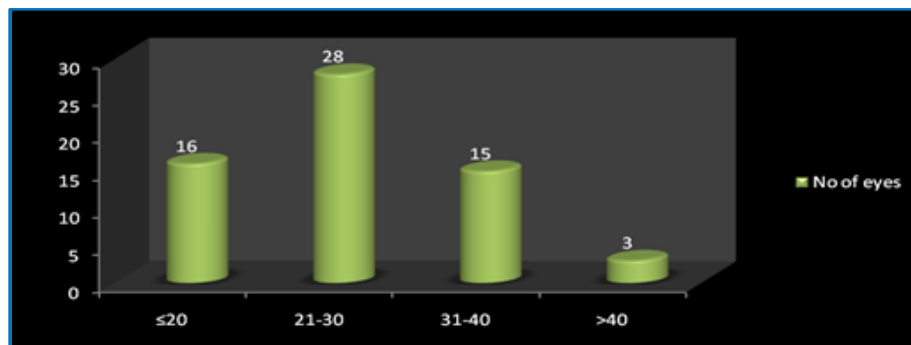
Graph 2: Status of Presence of Various Risk Factors

IOP in the study ranged from 12 – 50 mmHg. Mean IOP was 25.87 ± 8.4 mmHg. 16 eyes (25.81%) with IOP ≤ 20 mmHg belonged to glaucoma patients whose IOP was well controlled with medical management.

Majority of eyes (28; 45.16%) had IOP of 21-30 mmHg, with 15 (24.19%) having 31-40 mmHg and 3 eyes (4.84%) having IOP of > 40 mmHg.

IOP mm Hg	No. of eyes	%
≤ 20	16	25.81
21-30	28	45.16
31-40	15	24.19
> 40	3	4.84
Total	62	100.00
Mean	25.87 ± 8.4	

Table 3: Distribution of eyes by IOP mm Hg

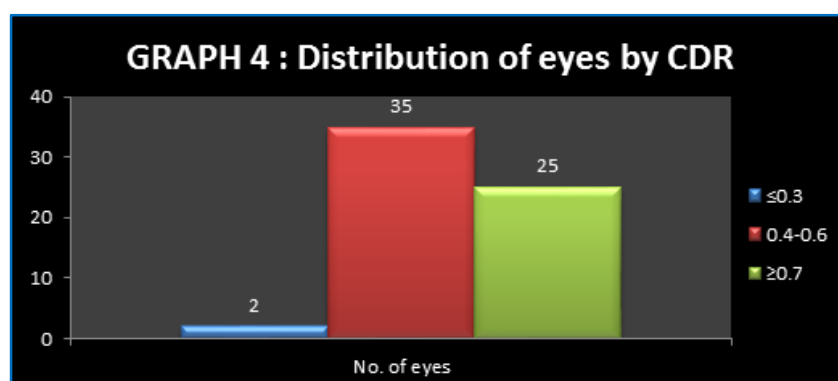


Graph 3: Distribution of eyes by IOP (mm Hg)

CDR	No. of eyes	%
≤ 0.3	2	3.23
0.4 – 0.6	35	56.45
≥ 0.7	25	40.32
Total	62	100.00

Table 4: Distribution of eyes by CDR

35 eyes (56.45%) had CDR of 0.4-0.6, 25 (40.32%) had ≥ 0.7 and 2 (3.23%) had ≤ 0.3 .



DISCUSSION: Out of 43 patients studied, mean age was found to be 55.95 ± 11 . Range was 32 to 80. Chandra et al.²⁹ in their study, found the mean age of the patients were 52.98 years [standard deviation (SD) =9.798] which correlates with our study. Suzuki et al.³⁰ in their study found the mean age of 119 POAG patients was 63.8 ± 12.0 years.

In the present study, there were nearly twice as many males (29; 67.44%) compared to females (14; 32.56%). Gyasi et al.³¹ had similar observation in their study where among the total of 446 POAG patients, number of males ($n=292$ [65.5%]) was almost twice compared to females ($n=154$ [34.5%]). Lin et al.²⁹ in their investigation showed that the number of male POAG patients was 2.55 times that of female POAG patients which also correlates with our study.

A family history of POAG is generally considered to be an important risk factor for POAG and having a first degree relative with glaucoma has been consistently associated with an increased risk of POAG. In the present study only 3 patients (6.98%) had a positive family history of POAG. In the Tajimi Study,³⁰ the information obtained in the interview with participants about the family history of glaucoma was also very less (5/119). The lack of awareness of glaucoma in rural and suburban population and errors in recall of the family history of glaucoma may explain the low yield in this study.

People with DM are more prone to POAG and diabetics tend to have higher IOP compared to non-diabetics. In this study, 13 patients (30.23%) were having diabetes mellitus. Lin et al.²⁹ found that 30.2% of patients had diabetes mellitus in their study group of 76,673 POAG patients which is similar to the results obtained in the present study. Jau- Der Ho et al. in their study of 4032 patients with POAG found that 1043 patients (25.9%) gave a positive history of diabetes

mellitus. Systemic hypertension may be associated with POAG as the capillary circulation at the disc may be more precarious in hypertensive. In our study, 12 patients (27.91%) had hypertension. Lin et al.²⁹ study of 76,673 POAG patients found that more than half (50.5%) of patients had hypertension. Jau- Der et al. in their study, found that 1968 patients (48.8%) had a positive history of hypertension out of 4032 POAG patients.

Intraocular pressure is the most significant risk factor for POAG and indeed the only one that can be currently modulated. The mean IOP in the present study was found to be 25.87 ± 8.4 mm Hg. 16 eyes (25.81%) with $IOP \leq 20$ mmHg belonged to glaucoma patients whose IOP was well controlled with medical management. On studying the distribution of IOP across 62 eyes, more number of eyes (45.16%) were found to have IOP in the range of 21 to 30 mmHg. There were 5 smokers (11.63%) and 1 (2.32%) myopic in the study.

CONCLUSION: Primary Open Angle Glaucoma is typically asymptomatic until significant visual field loss has occurred. As a leading cause of irreversible blindness worldwide, affecting more than 6.6 million people, blindness due to glaucoma is a mounting problem of global public health importance.

Glaucoma related blindness is largely preventable through timely diagnosis, effective treatment and ongoing monitoring. Timely diagnosis - the first step - requires in depth knowledge of demographical aspects of glaucoma, namely the risk factors.

This study is one such attempt to know more about the risk factors of POAG.

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AUTHORS:

1. Y. B. Bajantri
2. Rajshekar D
3. Madhuri Parande
4. Hemalatha A
5. Sneha N. Hegde

PARTICULARS OF CONTRIBUTORS:

1. Professor & HOD, Department of Ophthalmology, KIMS, Hubli.
2. Assistant Professor, Department of Ophthalmology, KIMS, Hubli.
3. Post Graduate Resident, Department of Ophthalmology, KIMS, Hubli.

4. Post Graduate Resident, Department of Ophthalmology, KIMS, Hubli.
5. Post Graduate Resident, Department of Ophthalmology, KIMS, Hubli.

NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Y. B. Bajantri,
Professor & HOD,
Department of Ophthalmology,
KIMS, Hubli.
E-mail: yalap5555@gmail.com

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