STUDY OF OCULAR RISK FACTORS FOR PRIMARY OPEN-ANGLE GLAUCOMA

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ABSTRACT

PURPOSE

Glaucoma causes irreversible progressive visual impairment. Increased intraocular pressure remains an important primary and prognostic risk factor for primary open-angle glaucoma (POAG), but its association with other risk factors is also present. This study was conducted to assess the relationship between potential ocular risk factors and the development of POAG to aid in early diagnosis.

DESIGN

Hospital based case control study.

METHODS

A case control study was conducted on 134 cases of POAG (Group 1) and 134 normal individuals without POAG (Group 2). Ocular risk factors like axial length, central corneal thickness, intraocular pressure, iris colour, cup-disc ratio, refractive status of eye were studied in both the groups and compared using Chi-square test.

RESULTS

POAG cases (Group 1) had thin cornea ($p=0.005$) and longer axial length ($p<0.05$) as compared to Group 2. Myopia ($p=0.268$) was more common than hypermetropia in POAG cases with odds ratio higher than unity (odds ratio=3.03).

CONCLUSION

A thin cornea and longer axial length were proved as ocular risk factors for POAG. Iris colour is not collaborative as risk factor. Myopia was more common in POAG cases.

KEYWORDS

POAG, Corneal Thickness, Axial Length, Myopia, IOP.

HOW TO CITE THIS ARTICLE: Garg P, Jha M, Singh L et al. Study of ocular risk factors for primary open-angle glaucoma. J. Evid. Based Med. Healthc. 2016; 3(24), 1064-1067. DOI: 10.18410/jebmh/2016/244

INTRODUCTION: Glaucoma is the second most frequent cause of blindness in the world after cataract.[1] As it causes irreversible visual impairment hampering day-to-day work, it has become a major public health problem.[2] Being asymptomatic up to the very advanced stage, it is also known as 'silent killer' of vision.[3,4] Primary open-angle glaucoma (POAG) is defined as 'a progressive, chronic optic neuropathy where intraocular pressure (IOP) and other currently unknown factors contribute to damage and in which, in the absence of other identifiable causes, there is characteristic acquired atrophy of the optic nerve and loss of retinal ganglion cells and their axons. There is associated open anterior chamber angle on gonioscopy.[5] Its inheritance is multifactorial and polygenic[6] and occurs in elderly and tends to run in families. Of the total 60 million persons affected by glaucoma, 11.2 million cases are estimated from the Indian subcontinent.[7,8] Over 2 million people develop POAG every year, worldwide.[9] The reported prevalence for primary open-angle glaucoma (POAG) varies between 1.62% and 3.51%.[8] Risk for blindness from primary open-angle glaucoma is high because of advance stage at the time of diagnosis, onset of glaucoma at young age, inadequate intraocular pressure control, high rate of progression despite treatment, undiagnosed glaucoma and missed opportunities for diagnosing glaucoma.[10] Increased intraocular pressure (IOP) remains an important primary and prognostic risk factor for POAG, but other IOP independent risk factors may be involved in the pathogenesis and progression of POAG.[11] Several ocular risk factors (viz. axial length, central corneal thickness,' intraocular pressure,' iris colour, cup-disc ratio, refractive status of eye) have been mentioned in different studies for development and progress of POAG; but a common consensus about certainty of several of them is still missing. The present study was conducted to assess the

Submission 23-02-2016, Peer Review 08-03-2016,
Acceptance 16-03-2016, Published 23-03-2016.
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DOI: 10.18410/jebmh/2016/244

relationship between potential ocular risk factors and the development of POAG to help us in predicting or detecting the disease in advance and taking actions to prevent the grievous consequences.

MATERIALS AND METHODS: It was a hospital based case control study, carried out in the Department of Ophthalmology at Era's Lucknow Medical College and Hospital, Lucknow over 2 years from 2011 to 2013. All patients of age 40 years and above regardless of sex diagnosed as POAG were included in the study after the informed consent and ethical clearance. The POAG was defined as: a person having glaucomatous field defect, glaucomatous disc changes or ocular pressure of >= 21 mm Hg in the presence of an open angle in either eye[6]. Patients having occludable angle in either eye or any history of intraocular surgery were excluded. Age and sex matched normal individuals not having POAG or any other debilitating eye pathology were taken as control. History regarding age, gender, chronic tobacco intake, chronic alcohol intake, history of hypertension, diabetes, thyroid disease, history of systemic corticosteroid intake and family history of glaucoma was taken. Detailed clinical examination of the eyes including visual acuity using Snellen's / Landolt's broken ring chart, fundus examination by +90 D lens and indirect ophthalmoscopy was done. Other ocular examination like IOP measurement (by applanation tonometer), examination of angle of anterior chamber (by slit-lamp gonioscopy), visual field charting (by Humphrey Field Analyser), axial length of eye (by A-scan Biometry), Central corneal thickness (by Cirrus Zeiss optical coherence tomography) was done.

RESULTS: 134 cases of POAG (Group I) and 134 controls (Group II) were enrolled in the study. The number of POAG cases increased with age and were maximum in the age group of 60-69 years (36.6%) vide table 1. The sex distribution was almost the same in both the groups, 66(49.3%) males in group 1 and 60(44.8%) males in group 2. Majority of patients of group 1 had bilateral disease (n=119; 88.8%). Thus the total number of eyes with POAG studied were 253 eyes. Group 1 eyes had relatively thinner corneas as compared to group 2 (vide Table 2) and the difference between the distribution of thickness of corneas of the two groups is statistically significant (p=0.005). The odds ratio for thin corneas (corneal thickness<= 504 um) is 2.381.

Majority of subjects, irrespective of their group had brown eyes, 243(96.0%) in group 1 and 260(97.0%) in group 2 vide Table 3. None of the cases had heterochromia iridum.

Relatively longer axial length (24 mm to 26.99 mm) was present in the POAG cases (60.4%) as compared to control eyes (33.6%) and this difference is statistically significant. The odds of POAG were lower than unity and was significant statistically (p<0.05) for axial lengths between 21 to 23.99. The odds ratio was above unity for axial lengths between 24 to 26.99. All the subjects having axial length > 27 had POAG, thus showing a significant association (p=0.021). So, with increasing axial length, the odds of POAG increased significantly (vide Table 4).

Myopia/compound myopia was seen more in POAG eyes (34%) than the control eyes (29.5%) while hypermetropia/compound hypermetropia was seen more in control eyes (21.6%) than in POAG cases (20.9%). The difference in distribution of refractive errors between the groups is statistically insignificant (p=0.268). Among all types of refractive errors, myopia emerged as the only error having odds higher than unity (odds ratio=3.03) thus can be considered as a risk factor (vide Table 5).

Number / Age	POAG Cases		Control Group	
	Number (n=134)	%	Number (n=134)	%
40-49 yrs.	26	19.4	27	20.1
50-59 yrs.	35	26.1	34	25.4
60-69 yrs.	49	36.6	48	35.8
70-79 yrs.	20	14.9	21	15.7
≥ 80 yrs.	4	3	3	2.2

Table 1: Age distribution of study cases

(χ^2=0.207 (df=4); p=0.995)

Central Corneal Thickness (µm)	POAG Cases (n=253)		Control (n=268)		Significance of difference		
	No.	%	No.	%	χ^2	p	OR
≤ 504 µm	74	29.2	42	15.7	13.86	<0.001	2.22 (1.45-3.41)
505-567 µm	154	60.9	194	72.4	7.79	0.005	0.59 (0.41-0.86)
≥568 µm	25	9.9	32	11.9	0.566	0.452	0.81 (0.47-1.41)

Table 2: Central corneal thickness as a risk factor for POAG

Iris Colour	POAG Eyes		Control Eyes	
	Number (N=253)	%	Number (N=268)	%
Brown	243	96.0	260	97.0
Heterochromia Iridis	10	4.0	8	3.0
Heterochromia Iridum	0	0	0	0

Table 3: Colour of iris as a risk factor for POAG

χ^2=0.365 (df=1); p=0.546
OR=0.75 (95% CI: 0.29-1.93)

Axial Length (mm)	POAG Cases (n=253)		Control (n=268)		Significance of difference		
	No.	%	No.	%	χ^2	p	OR
<20	0	0	0	0	-	-	-
20 – 20.99	2	.8	8	3	3.329	0.068	0.70 (0.12-4.25)
21 – 21.99	8	3.2	36	13.4	17.76	<0.001	0.26 (0.05-1.23)
22 – 22.99	19	7.5	40	14.9	7.13	0.008	0.46 (0.26-0.82)
23 – 23.99	66	26.1	94	35.1	4.94	0.026	0.65 (0.45-0.95)
24 – 24.99	85	33.6	60	22.4	8.14	0.004	1.75 (1.19-2.59)
25 – 25.99	53	20.9	26	9.7	12.80	<0.001	2.47 (1.49-4.09)
26 – 26.99	15	5.9	4	1.5	7.29	0.007	4.16 (1.36-12.71)
≥27	5	2.0	0	0	5.348	0.021	-

Table 4: Axial length of eyes as a risk factor for POAG

Refractive Error	POAG Cases (n=253)		Control (n=268)		Significance of difference		
	No.	%	No.	%	χ^2	p	OR
Emmetropia [SE= (-0.5D) to (+0.5D)]	114	45.1	131	48.9	0.763	0.382	0.86 (0.60-1.21)
Myopia [SE <(-0.5 D)]	86	34	79	29.5	1.226	0.268	1.23 (0.85-1.78)
Hypermetropia [SE >+0.5 D]	53	20.9	58	21.6	0.037	0.847	0.96 (0.63-1.46)

Table 5: Refractive errors as a risk factor for POAG

SE – Spherical equivalent

DISCUSSION: Glaucoma is a disease entity in the disease control strategy of the VISION 2020 initiative. It is the second leading cause of irreversible blindness in the adult population in India.[8, 12] Several risk factors, both ocular and systemic have been mentioned in literature for development and progress of POAG,[11] but a common consensus about certainty of several of them is still missing. In our study, POAG was more common in cases having central corneal thickness below normal range (<=505 µm). The mean central corneal thickness in POAG cases was 515.3(SD +/32.6) µm while that of control group was 534.8 (SD±27.8) µm. This association is statistically significant (p=0.005). These observations were similar to findings of Yeshigeta Gelaw (2012),[13] OHTS[14] study and retrospective study by Herndon LW et al.(2004).[15] Also, Lesk et al.[16, 17] demonstrated that patients with thinner corneas showed significantly greater lamina cribrosa displacement on HRT. Thus, agreeing to the fact that thinner cornea is a risk factor for POAG.

Considering and evaluating the colour of iris as the risk factor for POAG, in the present study, majority of patients (96.0%) in POAG group and (97.0%) in control group had brown iris as expected genetically in human race. Therefore, iris colour is not collaborative as a risk factor for POAG. Also, there is no evidence in literature regarding association of iris colour with POAG.

Anatomical predispositions of any organ in the body is one important factor making it vulnerable to different pathological changes or ailment. Similarly, in eye, longer axial length is a risk factor for POAG. Significantly, higher proportion of group 1 cases (62.4%) had axial length of eye 24 mm /more while only 33.6% of control eyes had of >=24 mm axial length. The statistical analysis of the present study data on correlation of axial length of eye with POAG show that with increasing axial length, the odds of POAG increased significantly, which is in concordance with observations made in other studies like Naila Ali(2007),[18] Shamira A. Perera et al. (2010),[19] Liang YB et al.(2011).[20] Thus, the observations of the present study and the other studies reported in literature suggest that longer axial length of the eye is a risk factor for POAG.

On looking for the type of refractive error, we found that in POAG group, myopia was more common (34%) as compared to control group (29.5%); but statistically this difference was not significant (p=0.268). The observation of the present study is akin with findings of OHTS (ocular hypertension treatment study)[21] and the EMGT(early manifest glaucoma trial)[22] studies. On the contrary, Vikas et al. (2009),[14] Nilsa I. Loyo-Berrios et al. (2007),[23] Shamira A. Perera et al.(2010)[24] had shown a positive correlation of myopia with POAG. The observed association between myopia and POAG may be explained by a surveillance bias for POAG cases in cases of myopia.[23] In myopes, the disc may appear glaucomatous with larger diameters and greater cup to disc ratio.[23] This is in most likelihood of being interpreted as glaucomatous cupping resulting in an over diagnosis of POAG.[23] No refractive error can be taken with certainty, as a risk factor for POAG as statistical considerations of findings of the present study for association of refractive errors with POAG and foregoing discussion do not suggest any significant correlation of refractive errors with POAG.

CONCLUSION: A thin cornea and longer axial length were proved as ocular risk factors for POAG. Iris colour is not collaborative as risk factor. Myopia was more common in POAG cases but the comparison was statistically insignificant and hence cannot be taken as a risk factor for POAG with surety. More extensive studies with still bigger sample size may be warranted for further confirmation of inferences drawn in the present study.

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