Clinical Profile of Myopic Patients as a Risk Factor for Primary Open Angle Glaucoma - A Prospective Observational Study in Gorakhpur, Uttar Pradesh

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ABSTRACT

BACKGROUND

Myopia is a complex trait including both genetic and environmental factors as well as gene-environment interactions. It has been recognized as a risk factor for development of glaucoma. Both Myopia and raised IOP are known to increase mechanical stress at optic nerve head leading to glaucomatous nerve damage. This study intends to evaluate the clinical profile of myopic subjects and its correlation with Primary open angle glaucoma (POAG).

METHODS

A prospective observational study done from November 2019 to December 2020 after taking proper informed consent and ethical clearance. 164 eyes of 96 patients studied were divided into three groups, Group 1: low myopia (< -3.00D), Group 2: moderate myopia (-3.00 D to -5.75 D), Group 3: high myopia (≥ -6.00 D). A complete ocular examination was performed. Intraocular pressure was measured using Goldmann applanation tonometer. Visual field analysis using Humphrey automated perimetry was done in patients with suspected primary open angle glaucoma (POAG). Angle parameters and central corneal thickness (CCT) were measured using anterior segment optical coherence tomography (AS-OCT).

RESULTS

164 eyes of 96 Myopic subjects were studied with no dropout during study period. Mean age was 46.05 yr. (range: 25-75 yr.). The refraction ranged from -0.50 DS to -17.00 DS. There was no statistically significant difference between Intraocular pressure (IOP), Central corneal thickness (CCT), corrected IOP and Nasal and Temporal Trabecular-iris Angle (TIA) between male and female of same age group. Mean IOP and mean CCT were found to vary significantly with age and with higher degree of myopia. Corrected IOP, Nasal and Temporal TIA increase significantly with higher degree of myopia. Cup-disc ratio (CDR) was found to be significantly higher in patients with moderate to high degree of Myopia.

CONCLUSIONS

Myopia is an important risk factor for development of primary open angle glaucoma, with its incidence increasing in patients with moderate to high myopia.

KEYWORDS

Myopia, Primary Open Angle Glaucoma, Intraocular Pressure, Central Corneal Thickness, Trabecular Iris Angle

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BACKGROUND

Primary open angle glaucoma is a chronic progressive optic neuropathy, and it affects 44.1 million individuals worldwide.[1] It is the most reported type of glaucoma in population-based prevalence studies. There is a disproportionate burden of POAG in Asia, with Asians accounting for 53 % (23.5 million) of POAG cases worldwide.[1,2] Early detection of POAG is important in delaying the progression of the disease. Therefore, a better understanding of the interplay between major risk factors for POAG is crucial. It has been hypothesized that elevated IOP exerts mechanical stress on the optic nerve head (ONH) and lamina cribrosa, and its adjacent tissues.[3,4] In addition, IOP-induced strain may also disrupt axonal transport of trophic factors which are essential to the auto regulation and survival of retinal ganglion cells.[3,4,5] As lamina cribrosa is the site where retinal ganglion cell axons gather together before traversing to the brain,[6] excessive mechanical strain at this structure may initiate glaucomatous damage.[1,7] Myopia is a complex trait including both genetic and environmental factors as well as gene-environment interactions.[8,9]

High myopia in many cases is a genetically determined condition and irregular autosomal dominant and autosomal recessive inheritance is mostly seen. Sometimes, sex linked inheritance has been reported. The relationship between high myopia and POAG is indicated by the finding of an increased responsiveness to topical steroids in eyes with myopia more than 5 Diopters.[10] High myopia (> -6.00 D) is associated with an increased risk of pathological ocular complications and may lead to blinding disorders such as premature cataracts, glaucoma, retinal detachment, and macular degeneration.[11] Thus, high myopia is a major cause of legal blindness in many developed countries.[12] The prevalence of myopia varies across populations of different regions and ethnicities. Myopic eyes have longer axial lengths and deeper anterior chambers as compared to emmetropic eyes. The lamina cribrosa is thinner and shows greater deformability in eyes with myopia than in emmetropic eyes. This greater compliance will make the optic nerve head more vulnerable to small fluctuations in intraocular pressure and subsequent retinal ganglion cell damage. Eyes with myopia may thus have greater susceptibility for lamina cribrosa deformation which may lead to subsequent development of POAG.[6,13] Although IOP and myopia are both closely linked to mechanical strain and deformation of the lamina cribrosa, the inter-relationship between IOP and myopia on the risk of POAG has not been well studied. Our study intends to evaluate the clinical profile of myopic subjects and its correlation with POAG.

METHODS

This is a prospective observational study on 164 eyes of 96 Myopic patient ≥ 25 yrs. of age presenting to outpatient department of a tertiary care centre of Gorakhpur, Uttar Pradesh conducted over a period of 14 months from November 2019 to December 2020 after taking proper informed consent and ethical clearance. Patients with myopic astigmatism, mixed astigmatism, previously known glaucoma, secondary glaucoma, and mature cataract were not included in our study. Patients with other retinal diseases, anterior segment pathology, faint fundal reflexes and indeterminate refraction were excluded from our study.

All the patients underwent complete ocular examination including visual acuity, BCVA (Best corrected visual acuity) and refractive power assessment using Snellen's visual acuity chart. Slit lamp examination, retinoscopy, dilated fundus examination and gonioscopy was performed on all the patients. Intra-ocular pressure was measured using Goldmann applanation tonometer after instillation of 0.5 % proparacaine eye drops. Visual field analysis using Humphrey automated perimetry was done in patients with suspected primary open angle glaucoma (POAG). All the patients were subjected to Anterior segment optical coherence tomography (AS OCT) for quantitative assessment of trabecular iris angle (TIA) and central corneal thickness (CCT).

164 eyes of 96 patients were divided into three groups:

- Group 1: included patients with low myopia with refraction < -3.00 D
- Group 2: included patients with moderate myopia ranging from -3.00 D to -5.75 D
- Group 3: included patients with high myopia with refractive error ≥ -6.00 D

Diagnosis of POAG was made by presence of two parameters of following: IOP ≥ 21 mm Hg after correcting for CCT, CDR > 0.3 on fundus examination with glaucomatous optic nerve damage and visual field findings suggestive of glaucomatous changes.

Data Analysis

Values were presented as mean in standard deviation. Statistical analysis was done using SPSS (Statistical Package for Social Sciences) Version 16.0 Statistical Analysis Software. Chi Square test was used to find the significance of study parameters on categorical scale between two groups. One way analysis of variance (ANOVA) test was applied to compare means of the 3 groups. The level of statistical significance was set to be $p < 0.05$.

RESULTS

		No. of Subjects	Percentage (%)
Age	25 - 44 yr.	52	54.17
	45 - 64 yr.	30	31.25
	≥ 65 yr.	14	14.58
Sex	Male	41	42.71
	Female	55	57.29
Complaints	Defective vision	65	67.71
	Ocular pain	10	10.42
	Check of glasses	4	4.17
	Others	17	17.71
Awareness of glaucoma	Aware	4	4.17
	Unaware	92	95.83

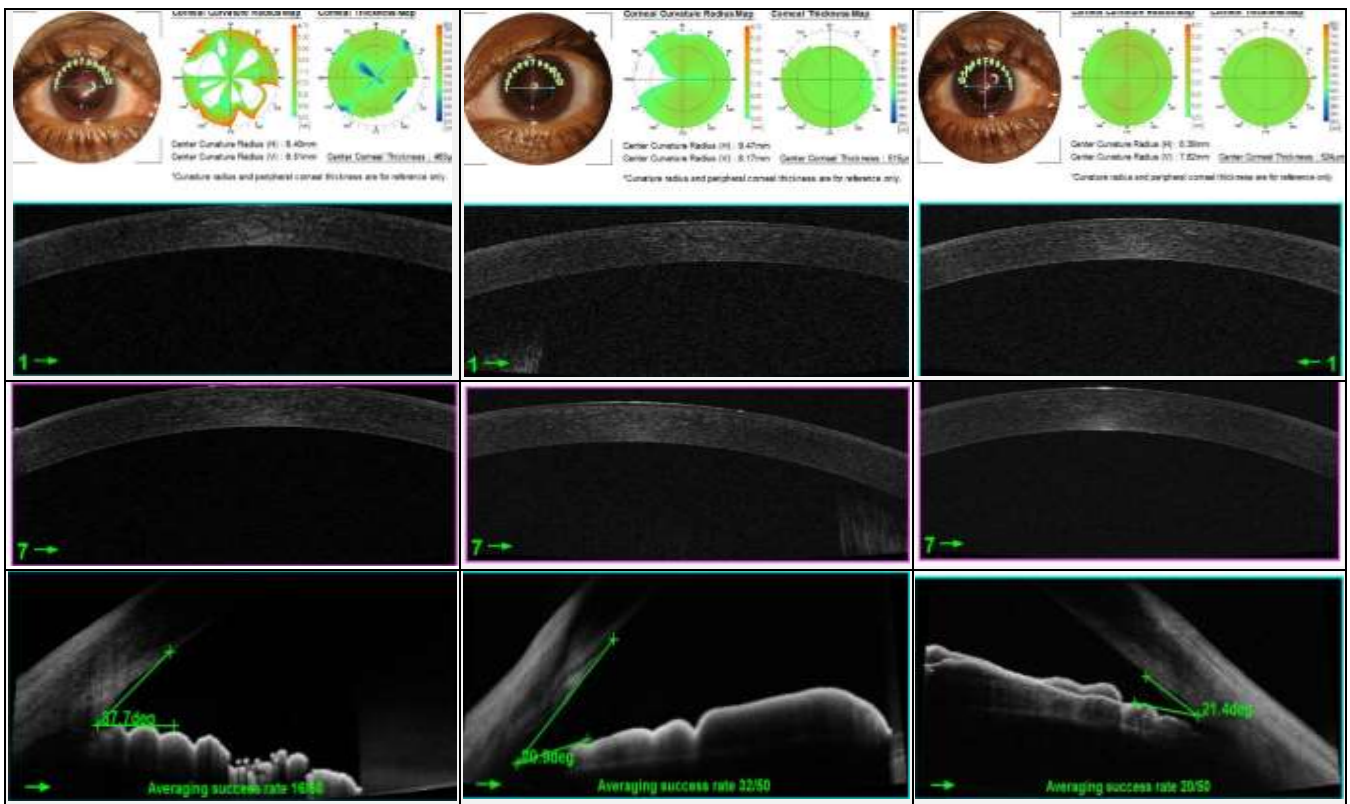
Table 1. Demographic Data

Sl. No.	Age	No. of Eyes	IOP (mm Hg)	CCT (µm)	Corrected IOP (mm Hg)	Nasal TIA (°)	Temporal TIA (°)
1.	25 - 44 yr	84	13.48 ± 3.92	551.86 ± 29.01	14.16 ± 4.48	28.17 ± 11.62	28.30 ± 11.40
2.	45 - 64 yr	55	14.99 ± 6.44	548.21 ± 28.86	15.89 ± 6.78	28.24 ± 11.18	27.95 ± 12.14
3.	≥ 65yr	25	16.36 ± 5.52	534.08 ± 25.46	16.65 ± 5.64	27.04 ± 11.74	26.30 ± 12.02
	p-value		.032	.025	.066	.898	.756

Table 2. Intraocular Pressure (IOP), Central Corneal Thickness (CCT), Corrected IOP, Nasal and Temporal TIA (Trabecular Iris Angle) According to Age

Sl. No.	Degree of Myopia	No. of Eyes	IOP (mm Hg)	CCT (µm)	Corrected IOP (mm Hg)	Nasal TIA (°)	Temporal TIA (°)
1.	Low	65	13.85 ± 4.36	543.57 ± 28.96	14.28 ± 5.06	26.54 ± 11.36	25.92 ± 11.98
2.	Moderate	50	13.25 ± 3.70	533.65 ± 28.14	13.97 ± 4.82	27.96 ± 11.53	27.39 ± 12.04
3.	High	49	16.13 ± 6.89	527.87 ± 26.7	16.64 ± 6.86	32.47 ± 11.18	32.17 ± 11.34
	p-value		.013	.012	.034	.021	.018

Table 3. Intraocular pressure (IOP), Central Corneal Thickness (CCT), Corrected IOP, Nasal and Temporal TIA (Trabecular Iris Angle) According to Degree of Myopia



Radial and Line Anterior Segment OCT of Subject with High Myopia | ***Radial and Line Anterior Segment OCT of Subject with Moderate Myopia*** | ***Radial and Line Anterior Segment OCT of Subject with Low Myopia***

Figure 1. Radial and Line Anterior Segment OCT findings in subjects with High, Moderate and Low Myopia Respectively.

Degree of Myopia	CDR 0-0.3	CDR 0.4-0.6	CDR ≥0.7	Total
Low	61	2	2	**65**
Moderate	43	3	4	**50**
High	35	5	9	**49**
p-value		.023		

Table 4. Relation of Cup Disc Ratio (CDR) to Degree of Myopia

Degree of Myopia	POAG	NO POAG	Total
Low	1	64	**65**
Moderate	3	47	**50**
High	8	41	**49**
p-value		.010	

Table 5. Relation of Primary Open Angle Glaucoma (POAG) to Degree of Myopia

A total of 96 Myopic subjects (164 eyes) were taken in our study with no dropout during the study period. Mean age of the study population was 46.05 yr. ranging from 25 yr. to 75 yr. The mean age of subjects did not vary significantly (p = .072) with mean age being 42.09 ± 11.91 for low myopia, 49.66 ± 14.81 for moderate myopia and 46.86 ± 13.77 for high myopia. The refractive error among the eyes included in our study ranged from -0.50 DS to -17.00 DS. Out of 164 Myopic eyes studied 9.76 % (n = 16) had uncorrected visual acuity > 6 / 24, after correction this was raised to 76.83 % (n = 126). Percentage of eyes with visual acuity between 6 / 24 – 3 / 60 reduced from 64.63 % (n = 106) to 14.63 % (n = 24) after refractive correction. Unaided visual acuity of < 3 / 60 was in 25.61 % (n = 42) of subjects this was reduced to 8.54 % (n = 14) after appropriate refractive correction.Examination of the 164 eyes showed that 26 eyes were diagnosed as either Primary open angle glaucoma (POAG) 12 (7.32 %), Chronic angle closure glaucoma (CACG) 4(2.43 %), Normal tension glaucoma (NTG) 2(1.22 %), ocular hypertension 5 (3.05 %), or glaucoma suspect 3(1.83 %). Visual field analysis of the 26 eyes revealed that 7 (26.92 %) eyes failed to produce a reliable field, 5 (19.23 %) were not subjected to the test from the start and only 8 (30.77 %) eyes showed visual field defects. Anterior chamber angle was 2-4 in 84.62 % (n = 22) and 0-1 in 7.69 % (n = 2). In the other 7.69 % (n = 2), it was open but there were peripheral anterior synechiae.

This was further confirmed by Anterior segment OCT findings.

Of the 12 eyes with POAG 3 (25 %) showed optic atrophy, 9 (75 %) had cup disc ratio ≥ 0.7 and 1(8.33 %) had pupils not reactive to light. 1(16.67 %) of the patients were smokers, 2(33.33 %) diabetics, 1(16.67 %) were hypertensive, 3(50 %) had a first degree glaucomatous relative while all of them gave a negative history of migraine.

Cup-disc ratio (CDR) was found to be significantly higher in patients with moderate to high degree of Myopia (p = .023). The incidence of POAG was found to be (1.54 %) in low myopia, (6 %) in moderate myopia and (16.33 %) in high myopia.

DISCUSSION

In our study the mean intraocular pressure (IOP) in mmHg was found to increase gradually and significantly with age (p=.032). Also, the mean IOP showed no significant difference between males and females of all the three age groups. Higher degrees of myopia were found to be significantly associated with higher mean IOP (p = .013). IOP being the most important risk factor for developing glaucoma, high myopes were found to be more prone to glaucoma than low or moderate myopes. This suggests that the relationship between glaucoma and myopia might be pressure mediated, the same result obtained by Nomura et al.[14] He found that IOP increased with advancing degrees of myopia, after adjusting for age and central corneal thickness.

The mean central corneal thickness (CCT) in µm was found to decrease gradually and significantly with age (p=.025). Nemesure et al[15] also reported an inverse relationship between CCT and age. The effect of age suggests age-related corneal biomechanical changes. Also, the mean CCT showed no difference between males and females in same age groups. The higher the degree of myopia the lesser was the central corneal thickness. The CCT in Myopic eyes were found to decrease significantly in eyes with moderate and high myopia (p = .012). This reflects that the central corneal thickness is a common determinant of myopia.[16] Nemesure et al[15] in his study suggested that CCT was directly related to refractive error, but high ametropia may bias the measurement of CCT.[17] Central corneal thickness (CCT) is also a known and an important independent risk factor for progression from ocular hypertension to early glaucoma (70 % Risk).

Higher degrees of myopia was also found to be significantly associated with higher mean corrected IOP, compared to moderate and low myopia (p = .034) in our study. The relationship between CCT and IOP is not linear, so even if the correction factor is applied, the correction of IOP over the extreme values of CCT can become inaccurate and thus not reliable. Also, none of the correction factors, so far proposed, has been universally accepted as a standard formula.

It was observed that the mean Nasal and mean Temporal TIA (Trabecular-iris angle) increased significantly with higher degree of myopia (p = 0.021; p = 0.018). The angle measured (in degrees) by gonioscopy correlated with TIA (in degrees) measured by Anterior segment OCT. This is comparable with the study of Khan N et al[18] as the study was conducted on general population while our study was conducted for a special group (myopes). This was also comparable with the study of Nolan WP et al where all patients who have closed angles on gonioscopy also showed closed angles on ASOCT.[19,20,21]

CDR ≥0.7 was found to increase significantly (p = .0239) in high myopia (18.37 %) compared to low and moderate myopia (3.08 % and 8.0 %). None of the studies related the degree of myopia to the CDR, but still CDR remains one of the parameters of glaucoma.

The relative incidence of POAG was (1.54 %) in low myopia, (6 %) in moderate myopia, and (16.33 %) in high myopia. Mitchell et al found it as 4.2 % in low myopia (-1 to -3D) and 4.4 % in moderate to high myopia (≥ -3D) compared to 1.5 % of eyes without myopia. A strong relationship between POAG and myopia was seen, with an odds ratio of 2.3 in eyes with low myopia (between -1.0 and -3.0D) and 3.3 in eyes with moderate-to-high myopia (> -3.0D). Mean IOP was approximately 0.5 mmHg higher in myopic eyes compared to nonmyopic eyes. The incidence in high myopia in his study was lower because he incorporated the moderate myopia with the high myopia[22]

In our study the relative incidence of primary open angle glaucoma in myopes was found to be 7.31 % (n = 12). Quigley et al estimated POAG as 0.97 %[23] and Jacob A et al estimated POAG as 0.41 %[24] in the general population. This indicates that myopes are at increased risk for developing POAG compared to the general population.

The relative incidence of chronic angle closure glaucoma was 2.43 % (n = 4), which is comparable to what was estimated in a study done in Cape town (2.3 %).[25] But, another study conducted in Vellore, India revealed a prevalence of 4.32 %, still they are comparable since ours was estimated in a special group (myopes) while the other in the general population. This reflects that CACG occur at a lower rate in myopes than in the general population.

The ratio of POAG (7.31 %): CACG (2.43 %) was 3.01:1; this is closer to Quigley study that estimated it in the general population to be 2.28 : 1 in Latin America and near east. In Africa, he estimated it as 150:1 and this is very far from our study and from what is observed in our daily practice. It seems that he greatly underestimated ACG occurrence in Africans. It is worth mentioning that ratios and percentages were obtained from new cases only, so they are expected to be even higher if old cases were taken into consideration.

Clinical examination of the 164 eyes revealed the diagnosis of POAG, CACG, OHT, NTG, and glaucoma suspect in 26 eyes. Those eyes were the ones subjected to visual field and gonioscopy. Visual field analysis of the 26 eyes showed that, 7 (26.92 %) eyes produced an unreliable field most probably because the test was carried after a period of waiting and when the patient reached its stage he had already been fatigued and lacking concentration. A thorough explanation of the procedure and the instructions were given to all patients before being subjected to the test. Perimetry should be repeated several times until the patient can produce a reliable one. 5 (19.23 %) were not subjected to

perimetry altogether either due to their very reduced corrected visual acuity or the patient was judged as being inattentive by the examiner.

The main purpose of this study is to find the relationship between the refractive errors and IOP and to confirm whether myopia, age and gender could be important risk factor for primary open angle glaucoma. In our study we found statistically significant difference in IOP as well as IOP after correcting for central corneal thickness among high myopics compared to other groups. Similar results were obtained by various other studies.[26,27,28,29] A significant increase in the IOP in high myopics (> -6D) in comparison to emmetropic, moderate myopic, low myopic and Hypermetropics was observed in these studies, indicating myopia as an important risk factor for ocular hypertension. Additionally, the association between refractive error and IOP was found to differ according to age However, no correlation was noted between intraocular pressure and refraction in some studies.[30] The possible mechanism for raised IOP in myopic subjects is the shearing forces exerted by scleral tension across the lamina cribrosa and may be important in pathogenesis of pressure related damage.[31] Myopic eyes have higher scleral tension across the lamina cribrosa than in the eyes with shorter axial length, even when IOP measured is the same.

Fluorescein angiographic studies have suggested a reduced choroidal blood flow in myopes, and the amplitude of the ocular pulse is lower in myopes than in emmetropes or hypermetropes.[32] The circulation to optic disc in myopic eye is also reduced and therefore myopics are more susceptible to raised IOP as suggested by Edward S Perkins and Charles Phelps. Morphologic optic nerve head changes often associated with myopia can mimic or mask glaucomatous changes complicating diagnosis and monitoring.

The main limitation of this study would be that the corneal curvature and axial length were not taken into account. Therefore, the role of these factors in the refraction related changes of the corneal morphology is not known. These factors may influence the correlation between myopia, intraocular pressure, and biomechanical properties of cornea. The other limitation is that the investigative groups are not age or gender matched which may influence the results. However, no significant differences were found between the females and males in each group. A large sample size with age and gender match and measurement of corneal biomechanical parameters needs to be considered in the study design in the future.

CONCLUSIONS

Myopia is an important risk factor for development of primary open angle glaucoma, with its incidence increasing in patients with moderate to high myopia. Screening for myopia and follow up with measurement of intraocular pressure, central corneal thickness, cup-disc ratio, visual field analysis and making available the advanced diagnostic equipment can aid in early diagnosis and hence treatment of glaucoma in order to prevent blindness and visual impairment in glaucomatous patients.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.
Financial or other competing interests: None.
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