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When We'' Suspect ""A Highly Myopic Patients Need to Start Glaucoma Medications

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Abstract

Background: Globally, glaucoma is regarded as one of main causes of blindness that is irreversible in adults. One of major risk factors for primary open angle glaucoma (POAG) is raised intraocular pressure. Glaucoma is sometimes difficult to be diagnosed during early stages because of varying causes and multiple patterns of clinical presentation. Glaucoma is one of the complications that associate myopia, a disease of the eye that has both environmental and genetic bases.
Aim of the study: The aim of this study is to focus on the findings implicating as indicators for beginning of glaucomatous changes in young myopic.
Patients and methods: this cohort study was carried out in Al-Diwaniyah province, mid-Euphrates region of Iraq,starting from April 2016 through June 2020. Forty five patients were enrolled in this study, a total of 78 eyes, with an age range of 4 to 20 years. The range of myopia spherical equivalent (SE) was ranging from (-6) to (-14) diopter. Patients were examined every 6 months for about 4 years and the clinical assessment included intraocular pressure (IOP), fundoscopy and visual field examination. The main objective was to make an idea about when to administer glaucoma medications to patients with high myopia when IOP measurement alone is not helping.
Results:B-zone atrophy, rim changes and nasalization of blood vessels were significantly associated with higher degree of myopia ($P < 0.05$), both individually and as a whole. B-zone atrophy was significantly associated with higher degree of myopia ($P < 0.05$); however, neither Rim changes nor Nasalization of blood vessels were significantly associated with higher degree of myopia, despite being more frequent ($P > 0.05$); however, taken all together fundoscopic changes were significantly associated with higher degree of myopia ($P < 0.05$).
Conclusions: It's more likely to initiate treatment in young myopes as progressive changes in the optic disc are noticed; because the patients with pathological myopia can't risk additional loss, on the other hand most of the eye examined had normal range intraocular pressure with an abnormal looking optic disc.
Keywords: high myopia, glaucoma, IOP(intraocular pressure)

Introduction

When intraocular pressure is high (> 20 mmHg) in the presence of moderate to high myopia, the risk of developing primary open angle glaucoma (POAG) is approximately 4.3 in comparison to eyes with lower IOP and without myopia (1). It is thought that optic disc in myopic eyes is more vulnerable to damage attributed to glaucoma as a result of intrinsic defects in the connective tissue structure and arrangement (2-4). Studies that are population based have shown that with higher degrees of myopia, the risk of glaucoma becomes greater (3). The task of distinguishing glaucoma from glaucomatous disorders is not easy and thus follow up with detailed fundoscopy, perimetry and optical coherence tomography (OCT) are necessary to differentiate between them (5). Increasing categories of myopia are associated with a higher risk factor for optic disc neuropathy and glaucoma like visual field defect (6, 7). In pediatric age group, the intraocular pressure (IOP) can be greater in myopic eyes when compared to non-myopic eyes; however, whether abnormal eye growth of childhood myopia is due to high IOP or due to myopia itself requires further investigations and research workin the existence of baseline data (8).

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In the presence of sufficiently elevated sclera compliance, “axial elongation in association with normal-range IOP” refers to happening of attacks of raised IOP during usual activates including sleeping with prone position, rubbing of eyes, and heavy exercise and these attacks would have the ability to augment stretching of the fundus and axial elongation (9).The cause of myopic progression and increased scleral compliance leading to increased susceptibility to axial elongation whether due to pathology of myopia or due to distending force of raised IOP is in need to be clarified (9).

From histological perspective, ocular rigidity is getting less with high axial length owing partly to scleral thinning secondary to stretching. Ocular rigidity also is less with less IOP and changes in response to diurnal variation in IOP. Therefore, in myopic eye, these responses may be a possible explanation as myopic eye may fail to retain pre-stress state (9).

One of the principal causes of poor vision in daily ophthalmological practice is myopia. The progression of myopia is dominated by axial elongation. The pathology may be attributed to reduced collagen synthesis, tissue loss, altered collagen fibers, increased matrix metalloproteinase activity and altered proteoglycan (9).A multitude of mechanisms has been introduced to highlight the relation between myopia and POAG such as the dominant participation of shearing forces in damaging head of optic nerve and raisedvulnerability of the optic nerve head to damage by high IOP (10, 11).

Myopia may be associated with a potentially blinding disorder which is glaucoma that involves degeneration of ganglion cells in the retina in a progressive manner (11). For early recognitionof structural alterations in association with glaucoma, retinal nerve fiber layer (RNFL) examination is essential (12). Optical coherence tomography (OCT) has shown that myopia is associated with temporal thinning and displacement of the inferior and superior nerve fiber layer bundles. Especially, increasing incidence of high myopia at younger ages have been observed in sequential generations of 'Asian' ethnicities, accompanied sometimes by visual field defects despite normal IOP (13).

Patients and methods

The current observational prospective cohort study included 45 patients age from 4 to 20 years, a total of 78 eyes, form the pool of patientsattending ophthalmology department for usual glass and refractive error examination. Data about the other eye of 12 patients were excluded because these eyes were severely damaged(or submitted to surgery).

Comprehensive ophthalmological examination was offered to all participants including thorough medical history, measuring best corrected visual acuity, slit lamp biomicroscopy,Goldmann applanation tonometry “IOP measurement for those below 8 years done by air puff applanation technique”, dilated fundoscopic examination using a90 or a 78 (D) diopter lens, visual field examination using octopus,laser iterferometry (HRT) done but the data obtained in case of high myopia were limited. Perimetry,VF testing excluding those who are pseudophakic and patients with other neurologic and ophthalmological problems. The range of myopia spherical equivalent (SE) was ranging from (-6) to (-14) diopter.

This study was carried out in Al-Diwaniyah province, mid-Euphrates region of Iraq, starting from April 2016 through June 2020. Patients were examined every 6 months for about 4 years and the clinical assessment

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included intraocular pressure (IOP), fundoscopy and visual field examination. The main objective was to make an idea about when to administer glaucoma medications to patients with high myopia when IOP measurement alone is not helping.

Ethical approval was issued by the ethical approval committee of the health institute in the province and verbal consent was obtained from parents of all participants.

Data were analyzed using statistical package for social sciences (SPSS) version 23 (IBM, Chicago, USA). Categorical data were expressed as number and percentage, whereas, quantitative data were expressed as mean, standard deviation and range. Chi-square test, Yates correction and Fischer exact testswere used to study association between categorical variables. The level of significance was set at $P \leq 0.05$.

Results

The current study included 45 patients with an age range of 4 to 20 years, a total of 78 eyes. The IOP and degree of myopia according to age are shown in table 1. In patients younger than 10 years, the association between degree of myopia and IOP is highly significant ($P< 0.01$). In addition, in patients older than 10 years, the association between degree of myopia and IOP is significant ($P< 0.05$). During four years of follow up, the changes in IOP were not significant in association with age and degree of myopia, as shown in table 2.

The association between degree of myopia and examination findings according to fundoscopy are demonstrated in table 3. B-zone atrophy, rim changes and nasalization of blood vessels were significantly associated with higher degree of myopia ($P < 0.05$), both individually and as a whole.

Fundoscopy changes over period of follow up (4years) are shown in table 4. B-zone atrophy was significantly associated with higher degree of myopia ($P < 0.05$); however, neither Rim changes nor Nasalization of blood vessels were significantly associated with higher degree of myopia, despite being more frequent ($P> 0.05$); however, taken all together fundoscopic changes were significantly associated with higher degree of myopia ($P< 0.05$). The frequency distribution of patients according to findings of Heidelberg Retina Tomograph (HRT) and visual field are shown in table 5 and these were done for those with noticeable changes in fundoscopy during period of follow.

Table 1: Degree of myopia versus IOP level

Age (years)	**IOP (mmHg)**	**Myopia (Diopter)**		***P*-value**
		(-6) to (-14)	**> (-14)**	
4 to 10	**< 12**	0	3	< 0.01 F HS
	12 - 17	22	0	
	18 - 21	0	4	
	> 21	0	2	
11 to 20	**< 12**	0	2	< 0.05 Y S
	12 - 17	33	0	
	18 - 21	4	3	

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	> 21	0	5	

IOP: intraocular pressure; **F**: Fischer exact test; **Y**: Yates correction; **HS**: highly significant; **S**: significant

Table 2: IOP follow over 4 years

Degree of myopia	Age years	IOP follow up	*P*-value
(- 6) to (-14)	(4 - 10)	+(-3)	>0.05 Y NS
	(Up to 20)	+(-5)	
> (-14)	(4 - 10)	+(-3)	> 0.05 Y NS
	(Up to 20)	+(-3)	

IOP: intraocular pressure; **F**: Fischer exact test; **Y**: Yates correction; **NS**: not significant

Table 3: Degree of myopia versus fundoscopy

Fundoscopy	Total *n* = 78	Myopia (-6) to (-14) D *n* = 59	Myopia > (-14) *n* =19	*P*-value
B-zone atrophy	11 (14%)	4 (6.8 %)	7 (36.8 %)	< 0.05 Y S
Rim changes	7 (8.9%)	2 (3.4 %)	5 (26.3 %)	< 0.05 Y S
Nasalization of blood vessels	5 (6.4%)	1 (1.7 %)	4 (21.1 %)	< 0.05 Y S
Total	23 (29.5%)	7 (11.9 %)	16 (84.2 %)	< 0.01 C HS

Y: Yates correction; **C:** Chi-square test; **HS**: highly significant; **S**: significant

Table 4: Fundoscopy changes over period of follow up (4years)

Fundoscopy	Total *n* = 78	Myopia (-6) to (-14) D *n* = 59	Myopia > (-14) *n* =19	*P*-value
B-zone atrophy	6 (7.7 %)	2 (3.4 %)	4 (21.1 %)	< 0.05 Y S
Rim changes	3 (3.8 %)	1 (1.7 %)	2 (10.5 %)	> 0.05 Y NS
Nasalization of blood vessels	3 (3.8 %)	1 (1.7 %)	2 (10.5 %)	> 0.05 Y NS
Total	12 (15.4 %)	4 (6.8 %)	8 (42.1 %)	< 0.01 Y HS

Y: Yates correction; **HS**: highly significant; **NS**: not significant; **S**: significant

Table 5: Heidelberg Retina Tomograph (HRT) and visual field (done for those with noticeable changes in fundoscopy during period of follow)

Degree of myopia	HRT *n* = 13	VF *n* = 26	Total *n* = 39
(-6) to (-14)	4	11	15
> (-14)	4	9	13

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Total, *n* (%)	8 (61.5 %)	20 (76.9 %)	28 (71.8 %)

n: number of eyes; **HRT**: Heidelberg Retina Tomograph

Discussion

If neuroretinopathy keeps progressing despite normal IOP, acquired retinal degeneration that accompanies pathologic myopia will make a challenge. In this study, authors try to explain when to initiate anti-glaucoma medications to patients with myopia depending on posterior segment examination. According to Blue Mountains Eye Study, a famous frequently cited study, patients are going to be a suspect of glaucoma in the following settings: "Raised IOP,Optic disc or retinal axon fibers appearance rise possibility of glaucomatous injury, unexplained perimetry changes as those occur in glaucoma , angle changes and family history of severe glaucoma and other risk factors" (14).

The current study included 45 patients, a total of 78 eyes, as some eyes were excluded because of previous surgery, severely disfigured or being simple myopia. The study has focused on ophthalmological examination to find if there are any progressive changes, in particular on fundoscopy to detect the start of glaucoma. The changes in IOP over the period of follow up was unremarkable(+-3 to +-5); however, alterations inthe optic disc and retinal nerve fibers continue to progressand were consistent with those happening in glaucoma (23/78(29.5%). The cup may begin to enlarge by progressive posterior collapse, as the axon fibers loss continue, with distortion of the remaining viable nerve fibers.Vessels high way can usually be noticed in situations where the rimtissue "but not the overlying nerve head vasculature" has collapsed. The vasculature passing over the collapsed neural rim tissue appeared just like a "overpass, suspended over", with lack of contact with tissue beneath.

There are two kinds of peripapillary atrophy. The first one is the "alpha-zone peripapillary atrophy", which is often seen in myopic eyes with areas of hypopigmentation and hyperpigmentation as a typical temporal crescent without known effect on glaucoma. The other type, "beta-zone peripapillary atrophy", was more frequent and more extensive in eyes with glaucoma in comparison with eyes that are unaffected (more obvious in high myopia7 versus 4 in moderate type). This type of atrophyinvolves loss of retinal pigment epithelium and choriocapillaris, leaving justbig choroidal vessels and sclera leading to the characteristic white appearance near the disc margin (15). There is often a correlation between site of atrophy and defects in the visual field (16).Other signs that are less specific for glaucomatous alterationwerenarrowing of peripapillary retinal vessels, nasal displacement of the vessels and baring of the circumlunar vessels. The cup appears pale and deeply excavated with progressive damage. The alterations in rim are seen on temporal site, on examining the disc,principally recapitulating a narrowing that with passage of time acquire notching appearance.

Considering the association between glaucoma and myopia, following adjustment for gender, age and other contributing risk factors,high myopia is mainly accompanied by a very wide spectrum retinal degeneration, whereas, glaucoma targets the optic disc (17, 18).

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continuous changes of retinal pigment epithelium and its degenerationhappen in a variety of clinicalpatternall over the fundus. “Tessellated appearance related to haphazard distribution of retinal pigmented epithelium degeneration and variable light reflection may be appreciated even in young patients with high myopia when retinal pigment epitheliumattenuation surrounds the optic disc”. This hypo pigmented finding is described as peripapillary atrophy commonly the optic disc has an oval appearance en face and is referred as tilted disc (19).

In glaucoma Disc changes are characterized by progressive thinning of neuroretinal rim which is regarded by some authorsas the whole mark of glaucomatous optic neuropathy involving excavation of neuroretinal rim in addition toalteration inblood vessels direction resulting in increased cupping and pallor within the cup, with no associated pallor of neuroretinal rim, made most reliable indicators of glaucoma.

A large cup in a large disc may also be physiologic.This is best evaluatedby measurement of the diameter of the disc. A disc with optic disc drusen or coloboma must be taken into consideration, as it can lead to visual field loss but not on the basis of glaucoma.Finally, a clinical challenge is present when the myopic disc isexamined for possible glaucoma damage.The tilting, size, and accompanyinganatomicalalterations often preclude the capacity to be sure about the likelihood of glaucoma.

Among the studied group 45(78 eyes) patients 7 patients found have IOP >21 mmHg, 5 patients IOP <12 the range for the rest were (12-21mmHg) while findings related to glaucoma seen in studied group some of them with accepted IOP level.Is that high myopia with increased axial length may be accompanied by more sclera thinning , poor elasticity of the sclera lead to scleral tension across the optic nerve head and lamina cribrosa region these will deliver tension onretinal nerve fiber layer followed by nerve injury and atrophy give picture simulate that of glaucoma on the other hand decrease sclera rigidity make the eye (especially nerve fibers)more vulnerable to damaging effects of IOP even when it below risk value as in normal tension category. Among 78 eyes we examined and followed we caught 23 with increased suspension of glaucoma and hence saving their vision from further damage with concentrated dilated fundoscpopy. In Highly myopic eyes there is markedly enlarged peripapillary sclera ringcharacterized by absences of bruch membrane.

The ophthalmoscopic signs suggestive of glaucomatous optic nerve degeneration are as following (20):

- **Mechanical signs:** Large optic cup, Asymmetrical cups, Progressive enlargement of cup, Narrowing/notching of rim and Vertical elongation of cup
- **Vascular signs:** Disc hemorrhage, Nasal displacement of vessels, Baring of circumlinear vessels and Tortuosity of retinal vessels on the disc

Blood vessels nasalization happens in severely advanced glaucoma (5 among studied group), a situation in which the only structural support remains along the nasal rim because of advanced loss of temporal, inferior and superiorrim tissue (14). It can be detected easily in advanced cupping and difficult to be observed in early stages of disease.

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The best way for approving initiation of glaucomatous damage is Laser interferometry keeping in mind the coast and availability (61.5 validity) together with visual field(76.9).

Conclusion: Ophthalmologist must carefully examine the neuroretinal rim and its surrounding peripapillary vasculature and tissue and avoid considering the cup to disc (C/D) ratio as only indicator of optic nerve condition, in particular in young individuals who have high myopia.

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