Myopia and Glaucoma

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Editors

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Preface

The association between myopia and glaucoma has been the subject of many clinical trials and population-based studies. Most have suggested that moderate to high myopia is associated with increased risk of primary open-angle glaucoma (POAG) and normal-tension glaucoma. Diagnosis of glaucoma involves several factors, including the level of intraocular pressure, characteristics of structural changes in the optic disc and retinal nerve fiber layer or inner retina, and functional deterioration, i.e., visual field defects. However, the clinical diagnosis of glaucoma in highly myopic eyes may be difficult.

The optic discs of myopic patients are notoriously difficult to assess, especially those coexistent with tilted discs. The discs frequently appear glaucomatous with larger diameters, greater cup-to-disc ratios, and larger and shallower optic cups. With regard to visual field defects, myopic retinal degeneration, which is common in high myopias, may cause defects that mimic glaucomatous visual field defects. It is possible that such cases of high myopia may be misclassified or misdiagnosed as POAG. Myopia, especially in moderate to high myopia, tends to present with a thin retina and choroid as the elongation of the eyeball leads to stretching of the structures, causing them to appear thinner than normal. Despite new imaging technologies with reasonable sensitivity and specificity for detecting glaucoma, each technology has some challenges associated with it when assessing myopic eyes.

We hope that this book will provide good guidance to all clinicians for diagnosing and monitoring the progression of glaucoma in myopia, especially in high myopias. It is not only a review. Our aim is to create a reference book on how to understand myopia and glaucoma better by presenting our experts' long experience, and it thus includes many of our actual clinical studies. Research findings presented here may help in understanding the mechanisms or pathogenesis of myopic glaucoma. From clinical epidemiology studies of myopia, we knew that myopia is a growing public health problem, and its prevalence and severity are increasing in various parts of the world, particularly in Asia. Epidemiological studies have suggested that there is an "epidemic" of myopia in Asia. Numerous case series, case controls, and large population-based studies support the conclusion that there is an association between high myopia and POAG. We predict that there will be ongoing discussion and interest in this field among experts.

The course of disease in POAG with high myopia can be seen in long-term follow-ups, and common clinical features between them can be delineated only by analyzing a sufficient volume of patient data. In this book we would like to share our valuable experience through our clinical studies. This knowledge will narrow the vague area between high myopia and glaucoma for clinicians and researchers.

This book will be beneficial to all ophthalmologists both in medical school and in research centers of universities as well as in private or government hospitals and clinics. The book is written not only for ophthalmologists, however, but also will be a valuable resource for ophthalmic researchers, postgraduate students, and optometrists or certified orthoptists.

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Chapter 1
An Epidemiologic Perspective

Aiko Iwase

Abstract The prevalence rates of primary open-angle glaucoma (POAG) and myopia are reported in many population-based studies. The association between myopia and POAG was discussed based on the results of population-based studies, and the importance of myopia as a strong risk factor for POAG was emphasized. A recent increase in the prevalence rate of myopia likely will lead to a future increase in the prevalence rate of POAG.

Keywords Primary open-angle glaucoma • Myopia • Prevalence rates

1.1 Introduction

Myopia, which affects about 1.6 billion people worldwide, is expected to affect 2.5 billion people by 2020 [1] and is associated with many vision-threatening eye diseases [2]. In addition to severe impairment of visual acuity associated with excessive pathologic myopia [2], the myopic refractive error, if uncorrected, also can cause visual impairment by itself, while correction of the refractive error with spectacles, contact lenses, or refractive surgery may impose a considerable socio-economic burden on individuals and society. The association of myopia and glaucoma has long been discussed, and myopia has been identified as an independent and strong risk factor for primary open-angle glaucoma (POAG) [3].

Myopic eyes have longer axial lengths and vitreous chamber depths, and it seems reasonable that these eyes tend to have a more deformed lamina cribrosa contributing to higher susceptibility to mechanical damage [4–6]. The association or relationship between myopia and POAG has long been a subject of numerous hospital-based observational studies. While that study design can highlight a particular aspect of this association, those studies are prone to selection bias, which may obscure some important causal relationships between the pathologies. In this entry, the relationship between myopia and POAG is discussed based on the results of population-based studies.

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Table 1.1 Prevalence of myopia: summary data from previous population-based studies

Ethnicity	Country	Project	Age range (years)	Participation rate (%)	No. samples	Myopia (<−0.5 diopters)	Myopia (<−1.0D)	High myopia (<−5 D)	High myopia (<−6 D)
Caucasian	USA	Baltimore Eye Survey [24]	40 ≤	79.2	2,659	24.1	16.8	2.6	1.9
Caucasian	USA	Beaver Dam Eye Study [25]	43–86	83.1	4,926	26.2	26.5	3.8	
Caucasian	USA	National Health and Nutrition Examination Survey [26]	20 <	84.5	12,010	41.0	33.1	6.0	
Caucasian	Australia	Blue Mountain Eye Study [27]	49 ≤	82.4	3,654	15.5	12.6	1.8	
Caucasian	The Netherlands	Rotterdam Study [28]	55–95	79.7	5,673		17.6	4.0	
Caucasian	Australia	Melbourne Visual Impairment Project [29]	40≤	83	3,271	16.9	15.8	2.5	
Caucasian	Germany	Gutenberg Health Study [30]	35–74	92.9	13,959	35.1	26.2		3.5
Mongolian	Mongolia	(Hovsgol) [31]	40 ≤		1,617	17.2			2.7
Japanese	Japan	Tajimi Study [32]	40 ≤	78.1	3,120	41.8	32.5	8.1	5.5
Chinese	Taiwan	Shihpai Eye Study [33]	65 ≤	66.6	1,361	19.4	15.0	2.4	
Chinese	China	Beijing Eye Study [34]	40–101	83.4	4,319	21.8	16.9	3.3	2.6
Chinese	China	Handan Eye Study [35]	30 ≤	85.9	6,491	26.7		1.8	
Korean	Korea	Namil Study [36]	40 ≤		1,215	20.5			1.0
Chinese	Singapore	Tanjong Pagar Study [37]	40–79	71.8	1,232	38.7	28.0		6.9
Chinese	China	Liwan Study [19]	50 ≤		1,269	32.3			
Malaysian	Singapore	Singapore Malay Eye Survey [38]	40–80	78.7	3,280	30.5	20.0	3.9	
Indonesian	Indonesia	Sumatora [39]	41 ≤		358	34.1	26.1		1.7

Indian	India	Andhra Pradesh Eye Disease Study [40]	40 ≤	85.4	2,522	34.6		4.5	
Indian	Singapore	Singapore Indian Eye study [41]	40	75.6	3,400	28.0	20.4	4.1	
Indian	India	Central India Eye and Medical Study [42]	30<	83.1	5,885	17.0	13.0	1.8	0.9
Burmese	Myanmar	Meiktila Eye Study [43]	40 ≤	75.1	1,863	50.9	42.7		6.5
Indian	India	Chennai Glaucoma Study (rural) [44]	40 ≤	81.8	3,924	36.5			
Indian	India	Chennai Glaucoma Study (urban) [45]	40 ≤	80.2	3,850	23.2			
Iranian	Iran	The Yazd Eye Study [46]		90.4	2,098	36.5			2.3
Bengalese	Bangladesh	Bangladesh National Blindness and Low vision Survey [47]	30 ≤	90.9	1,1624	22.1	12.5	1.8	
Hispanic	USA	Proyecto VER [48]	40 <	72	4,774		18.0	2.5	
Hispanic	USA	Los Angeles Latino Eye Study [49]	40 ≤	82	6,357		16.8	2.4	
Hispanic	Spain	Segovia Study [50]	40–79	89.6	510	25.4			
Black	USA	Baltimore Eye Survey [24]	40 ≤	79.2	2,200	20.9			0.9
Afro-Caribbean	West Indies	Barbados Eye Study [51]	40–84	84	4,036	21.9			

1.2 Prevalence of Myopia

The prevalence rates of myopia have been reported to differ among ethnic groups. For example, Chinese and Japanese populations have higher prevalence rates of myopia than Caucasian, black, or Hispanic populations (Table 1.1). However, the prevalence rates of myopia also differ among the Asian countries. Both genetic and environmental factors have been implicated in the etiology of myopia [7, 8], and variations in genetic and environmental factors combined among ethnic groups should be mainly responsible for differences in the prevalence rates of myopia among countries. It is noteworthy that the prevalence rates of myopia and high myopia in Japanese are the highest in the world [9].

1.3 Prevalence of POAG

The prevalence rates of POAG reported in various countries are summarized in Table 1.2. The prevalence rates of POAG, which seem to be much less dependent on environmental factors than myopia, also differ among ethnic groups, i.e., African-American populations have the highest prevalence rates followed by Hispanic and Japanese populations. The prevalence rates of POAG generally are relatively low in Caucasians.

1.4 Relationship Between Intraocular Pressure and Refraction

Needless to say, high intraocular pressure (IOP) is a definitive risk factor for POAG. As summarized in Table 1.3, the distribution of IOP values also differs among ethnic groups with African-American and Caucasian populations having relatively higher mean values. Unexpectedly, there is a paucity of information on the relationship between refraction and IOP. In two population-based studies performed by the Japan Glaucoma Society (Tajimi Study and Kumejima Study), higher myopia was associated significantly with higher IOP [10, 11], which also agreed with the results reported in a large Japanese study [12] and a population-based study performed in Northern China (Beijing Eye Study) [13].

This significant correlation between IOP, the most important risk factor for POAG, and myopic refraction, another important risk factor for POAG, highlights the importance of refractive status in managing patients with POAG in Japan.

Table 1.2 Prevalence of OAG and NTG: summary data from previous population-based studies

Ethnicity	Country	Project	Age range (years)	Prevalence of OAG (crude)	NTG/OAG (%)	Prevalence of NTG (%) (crude)
Caucasian	UK	(Hollows and Graham) [52]	40–74	0.4	35.0	0.2
Caucasian	Ireland	Roscommon Glaucoma Survey [53]	50 ≤	1.9	36.6	0.7
Caucasian	USA	Baltimore Eye Survey [54]	40 ≤	**1.4**		
Caucasian	USA	Beaver Dam Eye Study [55]	43–86	2.1	32.0	
Caucasian	Australia	Blue Mountain Eye Study [56]	59 ≤	**3.0**		
Caucasian	The Netherlands	Rotterdam Study [57]	55–95	1.1	39.0	0.4
Caucasian	Italy	Casteldaccia Eye Study [58]	40 ≤	1.2	38.5	
Caucasian	Italy	Egna-Neumarkt Study [59]	40 ≤	2.0	28.6	0.6
Caucasian	Australia	Melbourne Visual Impairment Project [60]	40 ≤	**1.8**		1.4
Mongolian	Mongolia	(Hovsgol) [61]	40 ≤	0.4		
Mongolian	Mongolia	Kailu [62]	40 <	1.4	64.0	0.9
Japanese	Japan	Japan nationwide [12]	40 <	2.5	79.0	2.0
Japanese	Japan	Tajimi Study [63]	40 ≤	**3.9**	92.3	3.6
Japanese	Japan	Kumejima Study [64]	40 ≤	4.0	82.1	3.3
Korean	Korea	Namil Study [65]	50 ≤	3.6	77.8	2.8
Chinese	China	Beijing Eye Study [66]	40–101	2.5		
Chinese	**China**	**Handan Eye Study** [67]	**30 <**	**1.2**	**90.0**	**1.0**
Chinese	China	Liwan Study [68]	50–102	**2.1**	85.0	1.8
Chinese	Singapore	Tanjong Pagar Study [69]	40–79	**1.2**		
Malay	Singapore	Singapore Malay Eye Survey [70]	40–80	**2.5**	84.6	2.7
Bengalese	Bangladesh	Bangladesh Study [71]	35 ≤	1.2		
Thai	Thailand	(Rom Klao) [72]	50 ≤	2.3		
Indian	India	Aravind Comprehensive Eye Survey [73]	40 ≤	**1.2**	75.0	0.9

(continued)

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Table 1.2 (continued)

Ethnicity	Country	Project	Age range (years)	Prevalence of OAG (crude)	NTG/OAG (%)	Prevalence of NTG (%) (crude)
Indian	India	Andhra Pradesh Eye Disease Study (rural) [14]	40 ≤	**1.6**	63.0	1.0
Indian	India	West Bengal Glaucoma Study [74]	50 ≤	3.4		
Indian	India	Chennai Glaucoma Study (rural) [75]	40 <	**1.6**	67.2	1.1
Indian	India	Chennai Glaucoma Study (urban) [75]	40 ≤	**3.5**	82.0	2.9
Indian	Singapore	Singapore Indian Eye Study [76]	40	**1.3**	82.6	1.1
Burmese	Myanmar	Meiktila Eye Study [77]	50 ≤	**2.0**		
Hispanic	USA	Proyecto VER [78]	40 <	2.0	80.0	1.6
Hispanic	USA	Los Angeles Latino Eye Study [79]	40 ≤	**4.7**	82.0	3.9
Hispanic	Spain	Segovia Study [80]	40–79	2.0		
Multiethnic	South Africa	(Western Cape) [81]	40 ≤	1.5		
Multiethnic	West Indies	Barbados Eye Study [82]	40–84	7.1		
Black	West Indies	(St Lucia) [83]	30 ≤	8.8	36.0	
Black	USA	Baltimore Eye Survey [54]	40 ≤	4.2		
Black	Tanzania	(Kongwa District) [84]	40 ≤	3.1	75.0	
Black	South Africa	(KwaZulu-Natal) [85]	40 ≤	2.8	57.1	1.6

1.5 Myopia and POAG

Previous population-based studies have not always yielded consistent results regarding the relationship between myopia and POAG, while those performed in Asian countries including Japan have consistently found a significant association between myopia and POAG [14–20]. Marcus et al. [3] reported in a meta-analysis that the pooled odds ratio (OR) of the association between myopia and POAG was 1.92 (95 % confidence interval [CI], 1.54–2.38) based on 11 population-based

Table 1.3 IOP: summary of previous population-based studies

Ethnicity	Country	Study	Age range (years)	IOP
Caucasian	United Kingdom	(Hollows and Graham) [52]	40–74	15.9
Caucasian	Ireland	Roscommon Glaucoma Survey [53]	50 ≤	14.6
Caucasian	USA	Baltimore Eye Survey [86]	40 ≤	17.2
Caucasian	USA	Beaver Dam Eye Study [87]	43–86	15.3
Caucasian	Australia	Blue Mountain Eye Study [88]	59 ≤	16
Caucasian	The Netherlands	Rotterdam Study [89]	55–95	14.7
Caucasian	Italy	Casteldaccia Eye Study [58]	40 ≤	15.1
Caucasian	Italy	The Egna-Neumarkt Study [59]	40 ≤	15.1
Caucasian	Australia	The Melbourne Visual Impairment Project [60]	40 ≤	14.3
Mongolian	Mongolia	(Hovsgol) [61]	40 ≤	15.9
Mongolian	Mongolia	Kailu [62]	40 <	15.0
Japanese	Japan	Japan nationwide [12]	40 <	13.1
Japanese	Japan	Tajimi Study [63]	40 ≤	14.6
Japanese	Japan	Kumejima Study [11]	40 ≤	14.8
Korean	Korea	Namil Study [65]	50 ≤	13.5
Chinese	China	Beijing Eye Study [66]	40–101	16.1
Chinese	China	Handan Eye Study [90]	30 <	15.0
Chinese	China	Liwan Study [91]	50–102	15.2
Chinese	Singapore	Tanjong Pagar Study [92]	40–79	15.3
Malaysian	Singapore	Singapore Malay Eye Survey [93]	40–80	15.5
Bengalese	Bangladesh	Bangladesh Study [71]	35 ≤	15
Thai	Thailand	(Rom Klao) [72]	50 ≤	13.4
Indian	India	Aravind Comprehensive Eye Survey [73]	40 ≤	15.4
Indian	India	Andhra Pradesh Eye Disease Study (rural) [14]	40 ≤	14.5
Indian	India	West Bengal Glaucoma Study [74]	50 ≤	13.8
Indian	India	Chennai Glaucoma Study (rural) [75]	40 <	14.3
Indian	India	Chennai Glaucoma Study (urban) [75]	40 ≤	16.2
Indian	Singapore	Singapore Indian Eye Study (SINDI) [76]	40-	15.6
Burmese	Myanmar	Meiktila Eye Study	50 ≤	14.5
Hispanic	USA	Proyecto VER [94]	40 <	15.6
Hispanic	USA	Los Angeles Latino Eye Study [95]	40 ≤	14.5
Hispanic	Spain	Segovia Study [80]	40–79	14.3
Multiethnic	South Africa	(Western Cape) [81]	40 ≤	17
Multiethnic	West Indies	Barbados Eye Study [96]	40–84	18.1
Black	West Indies	(St Lucia) [83]	30 ≤	17.7
Black	USA	Baltimore Eye Survey [86]	40 ≤	16
Black	Tanzania	(Kongwa District) [84]	40 ≤	15.7
Black	South Africa	(KwaZulu-Natal) [85]	40 ≤	14.2

All participants or normal right eyes (male)

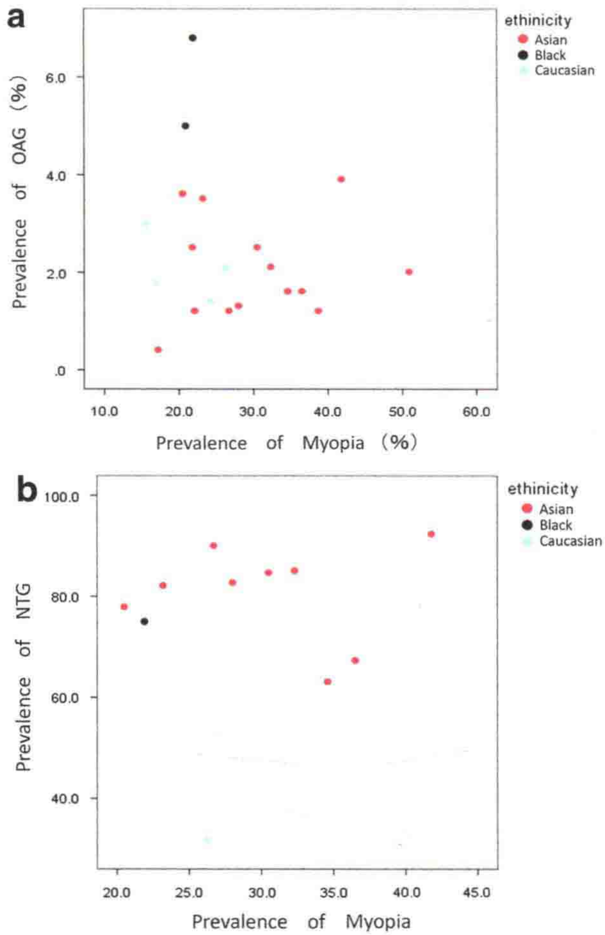

Fig. 1.1 (**a**) Prevalence of OAG versus prevalence of myopia. (**b**) Prevalence of NTG versus prevalence of myopia

studies, and the pooled ORs of the association between low myopia (> -3.0 diopters) and moderate to high myopia (≤ -3.0 diopters) were 1.65 (CI, 1.26–2.17) and 2.46 (CI, 1.93–3.15), respectively, based on seven population-based studies. The pooled ORs for low and moderate to high myopia were similar to those in the Tajimi Study, i.e., 1.85 (CI, 1.03–3.31) and 2.60 (CI, 1.56–4.35), respectively [16]. A significant relationship between myopia and POAG in Japanese patients also was confirmed by the Kumejima Study [11], in which the mean refraction was much less myopic than that in the Tajimi Study [20]. A large Swedish study [21] reported that the correlation between the prevalence rate of myopia and that of POAG was more evident in a subpopulation with IOP less than 15 mmHg, which suggested that the association between myopia and POAG would be more evident in the eyes with a normal IOP (normal-tension glaucoma [NTG]). A similar tendency also is seen in Fig. 1.1 where the prevalence rates of myopia reported in population-based studies are plotted separately against those of POAG and NTG (POAG with IOP < 22 mmHg at screening).

The prevalence of myopia has been increasing gradually worldwide. For example, the prevalence of myopia in US citizens aged 12–54 years was significantly ($P < 0.001$ for all comparisons) higher in 1999–2004 than in 1971–1972 (41.6 % vs. 25.0 %, respectively), in Caucasians (43.0 % vs. 26.3 %) and in African-Americans (33.5 % vs. 13.0 %) [22]. Further, the prevalence of myopia is higher in younger than older generations, which indicates that the prevalence of myopia in adult populations will increase further in the future [3, 9]. Since myopia is a strong risk factor for POAG, the increased prevalence of myopia should result in an increased prevalence of POAG in the future. POAG contributes to global blindness to a degree that is second only to cataract [23]. These facts clearly indicate the importance of determining in future studies the underlying pathology associated with myopia and POAG.

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