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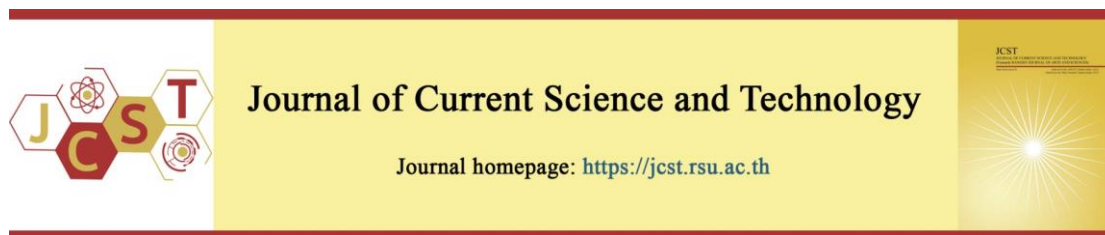
The relationship of refractive error and glaucoma in a university eye clinic

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Abstract

The Faculty of Optometry at Rangsit University performed a retrospective study using records from the eye clinic at Rangsit University (RSU) Healthcare. The objective of the study was to evaluate the relationships between refractive errors and glaucoma and between systemic diseases and glaucoma. Participants were patients attending the eye clinic between 2015 and 2019, aged 40-80 years, who had complete eye examinations and regular follow-up. The total number of subjects was 3,468 (mean age 60.19 ± 10.63 years). The examination included measurement of the presenting and best-corrected visual acuity, auto and manifest refraction, applanation intraocular pressure measurement, gonioscopy, cup-to-disc ratio, nerve fiber layer analysis, and perimeter and central corneal thickness measurement. Glaucoma was diagnosed via standardized criteria of the American Academy of Ophthalmology. Cases of refractive error, expressed as spherical equivalent (SE), included 1,154 cases of myopia (mild, moderate and severe), 1,381 cases of hyperopia (mild, moderate and severe) and 359 cases of astigmatism. Subjects also included 302 emmetropic individuals, 139 subjects with pseudophakia and 133 individuals who had undergone refractive surgery. A total of 555 glaucoma cases (19.56%) were identified, including 354 cases of primary open-angle glaucoma (POAG), 50 instances of primary angle-closure glaucoma (PACG), 106 cases of normotension glaucoma (NTG), and 45 cases of secondary glaucoma (SOAG). Subjects with glaucoma-related conditions included 41 post-glaucoma surgery cases, 81 ocular hypertension (OHT) cases, 186 primary open-angle glaucoma-suspect (POAGS) cases, 178 individuals with primary angle closure (PAC) and 166 subjects who had undergone laser peripheral iridotomy (LPI). The results indicated that the prevalence of some types of glaucoma and glaucoma-related conditions (PAC, NTG, OHT and SOAG) increased with advancing age ($p = 0.022, 0.001, 0.001, 0.021$ respectively). Relationships between refractive error and glaucoma subtypes were found. Mild, moderate and high myopia (-0.50 to -3.00 D, -3.25 to -5.00 D, and -5.25 D or greater, respectively) were correlated with POAG and NTG ($p = 0.001$). Mild and moderate hyperopia (+0.50 to +2.00 D and +2.25 to +5.00 D, respectively), were correlated with POAG and NTG ($p = 0.001$). PACG was correlated with mild, moderate and high myopia and mild to moderate hyperopia ($p = 0.001$). The lack of relationship between high hyperopia with PACG may be due to fact that 5.85 % of the studied population had already undergone laser peripheral iridotomy. Among glaucoma subtypes, NTG patients were most advanced in age (68.82 ± 10.73 years) and SOAG patients were the youngest ($58.36 \pm 13.88.79$ years). Compared to previous reports, our study revealed an increased glaucoma prevalence in individuals with myopia and hyperopia due to methodological differences and possibly due to our patients being older (60 years vs. 58 years). Diabetes was significantly correlated with SOAG ($p = 0.041$). Hypertension was not related to any type of glaucoma. Dyslipidemia was significantly correlated with SOAG ($p = 0.046$). In conclusion, this study found myopia and hyperopia to be related to an increased prevalence of all forms of open-angle glaucoma, including normal-tension glaucoma and angle-closure glaucoma, even after laser peripheral iridotomy. Diabetes and dyslipidemia were correlated with secondary open-angle glaucoma.

Keywords: angle-closure glaucoma; eye clinic; myopia; hyperopia; open-angle glaucoma; refractive error.

1. Introduction

Glaucoma refers to a group of ocular disorders that are related to progressive optic neuropathy. It is the most common cause of permanent or irreversible blindness worldwide (Quigley & Broman, 2006). The number of people with glaucoma worldwide in 2010 and 2020. Known risk factors include advanced age, family history (Kong, Chen, Chen, & Sun, 2011) and elevated intraocular pressure (IOP) found during an eye exam (Wong, Klein, Klein, Knudtson & Lee, 2003). Several large cross-sectional studies have reported a higher prevalence of primary open-angle glaucoma (POAG), the most common form of glaucoma, among myopic individuals compared with those without myopia, indicating that refractive error may play a role in the pathogenesis of glaucoma (Grødum, Heijl, & Bengtsson, 2001).

Compared with individuals of European descent, people of African ancestry are suspected to be at increased risk of developing POAG (Stein et al., 2011), whereas Japanese individuals have a higher incidence and prevalence of normal-tension glaucoma (NTG) and some East Asian populations may be more susceptible anatomically to primary angle-closure glaucoma (PACG; Nolan, 2007). Reasons for these racial differences are not known. A population-based study in Singapore found that individuals with moderate and high myopia (greater than -4.00 D) had a high prevalence of POAG (OR 2.87; 95% Confidence Interval 1.09-7.53). The role of refractive error in glaucoma has not been well studied in Thailand. The aim of this study conducted by the Faculty of Optometry is to assess the relationship between refractive error and the prevalence of glaucoma and glaucoma-related conditions. Open-angle glaucoma (POAG, NTG) and angle-closure glaucoma (PACG) included ocular hypertension (OHT). The correlation between glaucoma and some non-communicating systemic diseases were also studied.

2. Objectives

To study the relationships between refractive error and glaucoma and between certain systemic diseases and glaucoma.

3. Method

This study was reviewed and exempted by the Ethics Review Board of Rangsit University (exemption number RSUERB2020-041). We retrospectively reviewed records of patients who had presented to the eye clinic at Rangsit University's RSU Healthcare Clinic between 2015 and 2019.

Records selected for inclusion in the study were those of individuals aged 40-80 years who had undergone a comprehensive eye examination including documentation of visual acuity and refractive error measurement (auto and manifest), intraocular pressure (IOP) using the Goldmann applanation tonometer, Central Corneal Thickness (CCT) by optical coherence tomography (OCT; Zeiss, Cirrus 5000), corneal topography (Oculus), visual field by automated perimeter (Zeiss 750i), cup-to-disc ratio (CDR) data by direct ophthalmoscopy and fundus photography (KOWA VX 10i), and evaluation of the nerve fiber layer by OCT (Zeiss, Cirrus 5000).

Once we identified records of individuals aged 40-80 that included complete eye examination information as indicated, records of individuals with astigmatism, post-surgery pseudophakia, post-refractive surgery, eye disease-induced refractive error such as cataract nuclear sclerosis type, lens subluxation, computer vision syndrome with pseudomyopia and uncontrolled diabetes were excluded for possible myopia. Individuals with central serous chorioretinopathy and choroidal melanoma were also excluded for possible hyperopia.

Glaucoma was diagnosed using criteria from the American Academy of Ophthalmology (AAO) on the basis of gonioscopy, optic nerve defects and corresponding visual field loss, and intraocular pressure in some glaucoma-related cases. In this study, we used definitions of subtypes of glaucoma and glaucoma-related conditions per the AAO Preferred Practice Pattern (Gedde et al., 2021).

The "no glaucoma" group had no diagnosis of any type of glaucoma, no documented IOP of 22 mmHg or more in either eye and no interocular CDR difference of 0.2 or more.

Records listed with post-glaucoma surgery or post-laser peripheral iridotomy are documented here as "related glaucoma." No differences were noted between the right eye and the left eye in analysis, and in this report, we present findings for the right eyes.

4. Results

A total of 3,468 records of patients 40–80 years of age (mean 60.09 ± 10.65) were eligible for

the study. There were 1,544 male patients (mean age 59.97 ± 10.67 years) and 1,924 female patients (mean age 60.19 ± 10.63 years). Of these, 1,154 were myopic and 1,381 were hyperopic. Three hundred and two were emmetropic with glaucoma and used for comparison with individuals with glaucoma and refractive error. Excluded from analysis were records of 359 individuals with astigmatism, 139 with pseudophakia and 133 who had had refractive surgery (Table 1 and Figure 1).
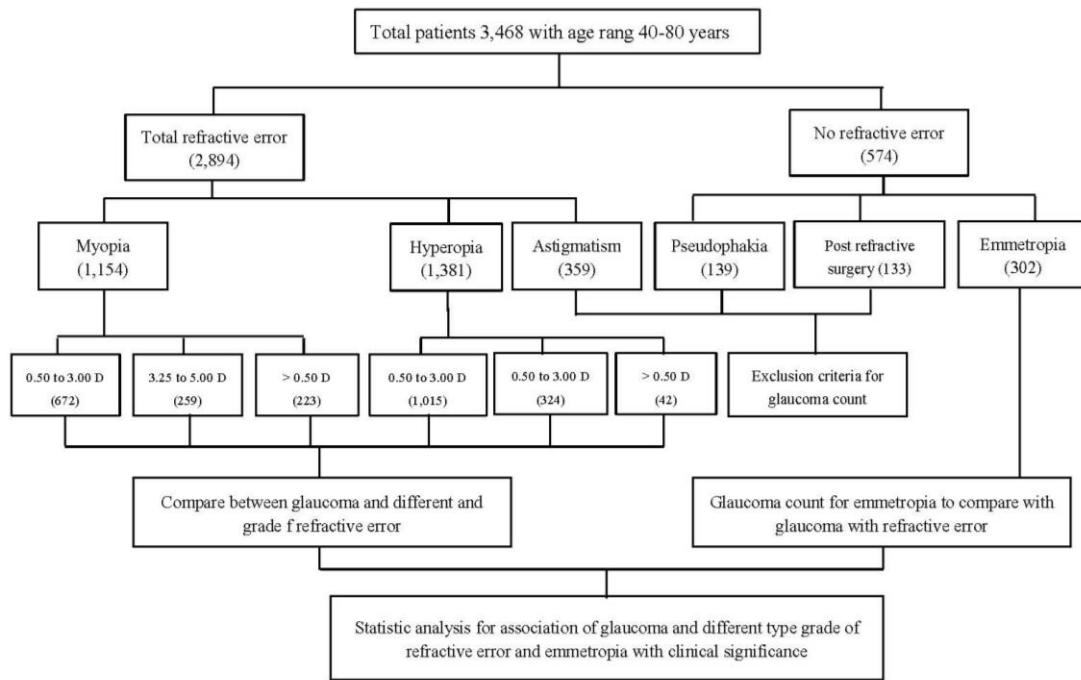

Figure 1 Conceptual framework of the study of refractive error and glaucoma
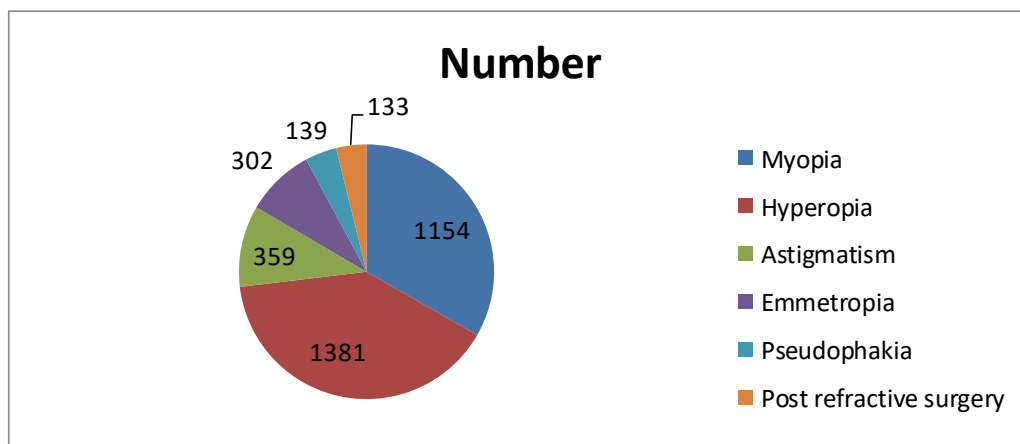
Figure 2 Pie chart illustrating total subjects with refractive error, emmetropia and exclusion groups

There were 555 patients diagnosed with glaucoma (19.56%), and subtypes were as follows: 354 had primary open-angle glaucoma (POAG), 106 had normal-tension glaucoma (NTG), 50 had primary angle-closure glaucoma (PACG) and 45 had secondary glaucoma (SOAG). Those with glaucoma-related conditions included 186 open-angle glaucoma suspects (POAGS), 81 patients with ocular hypertension (OHT), and 178 patients with primary angle closure (PAC). There were 41

postoperative glaucoma cases with an unknown subtype of glaucoma and 166 laser peripheral iridotomy cases consisting mainly of individuals with angle-closure glaucoma and narrow occludable angle (Table 1).

Table 1 Description of participants (demographic, refractive error, glaucoma and health profiles by age)

	Age range	40-50 yrs. (n =779)	51-60 yrs. (n =922)	61-70 yrs. (n=1,111)	71-80yrs. (n = 656)	Total (3,468)
Gender	Male (Number and Percent)	360 23.32%	395 25.58%	508 32.90%	281 18.20%	1,544
	Female (Number and Percent)	419 21.78%	527 27.39%	603 31.34%	375 19.49%	1,924
Refractive Error	Mild myopia -0.50 to -3.00 D (Number and Percent)	191 28.42%	166 24.70%	183 27.23%	132 19.64%	672
	Moderate myopia -3.25 to -5.00 D (Number and Percent)	62 23.94%	64 24.71%	90 34.74%	43 16.60%	259
	High myopia -5.25 D or less (Number and Percent)	72 32.29%	74 33.18%	62 27.80%	15 6.73%	223
	All myopia -0.50 D or less (Number and Percent)	325 28.16%	304 26.34%	335 29.03%	190 16.46%	1,154
	Mild hyperopia +0.50 to +2.00 D (Number and Percent)	173 17.04%	307 30.25%	349 34.38%	186 18.33%	1,015
	Moderate hyperopia +2.25 to +5.00 D (Number and Percent)	22 6.79%	66 20.37%	148 45.68%	88 27.16%	324
	High hyperopia +5.25 D and greater (Number and Percent)	10 23.81%	15 35.71%	12 28.57%	5 11.91%	42
	All hyperopia +0.50 D and greater (Number and Percent)	205 14.84%	388 28.10%	509 36.86%	279 20.20%	1,381
	Astigmatism (≥- 1.00 D) (Number and Percent)	69 19.22%	82 22.84%	110 30.64%	98 27.30%	359
	Emmetropia (+0.25 to -0.25 D) (Number and Percent)	121 40.07%	69 22.85%	69 22.85%	43 14.24%	302
	Pseudophakia (Number and Percent)	7 5.03%	21 15.11%	37 26.62%	74 53.24%	139
	Post refractive surgery (Number and Percent)	69 51.88%	26 19.55%	18 13.53%	20 15.04%	133
Glaucoma (Open angle)	Primary open-angle glaucoma (POAG)	56 15.82%	82 23.16%	110 31.07%	106 29.94%	354
	Normal tension glaucoma (NTG)	3 2.83%	20 18.86%	31 29.25%	52 49.06%	106
	Secondary glaucoma (SOAG)	16 35.56%	6 13.33%	15 33.33%	8 17.78%	45
Glaucoma (Angle closure)	Primary angle-closure glaucoma (PACG)	4 8%	11 22%	21 42%	14 28%	50
Glaucoma related	POAG suspect (POAGS)	42 22.58%	47 25.27%	58 31.18%	39 20.97%	186
	Post-Glaucoma Surgery	10	14	12	5	41

Age range	40-50 yrs. (n =779)	51-60 yrs. (n =922)	61-70 yrs. (n=1,111)	71-80yrs. (n = 656)	Total (3,468)
	24.39%	34.15%	29.27%	12.19%	
Ocular hypertension (OHT)	24	25	25	7	81
	29.63%	30.86%	30.86%	8.64%	
Primary angle-closure (PAC)	20	42	67	49	178
	11.24%	23.60%	37.64%	27.52%	
Laser peripheral iridotomy (LPI)	33	48	43	42	166
	19.88%	28.92%	25.90%	25.30%	
No glaucoma or related conditions	571	627	729	334	2,261
	25.25%	27.73%	32.24%	14.77%	
Systemic diseases Diabetes	108	109	175	134	526
	20.53%	20.72%	33.27%	25.48%	
Hypertension	13	19	23	15	70
	18.57%	27.14%	32.86%	21.43%	
Dyslipidemia	6	2	3	2	13
	46.15%	15.38%	23.08%	15.38%	

Among men with diabetes, 43 of 241 (17.84%) had glaucoma; among men with hypertension, 9 of 37 (24.32%) had glaucoma; among men with dyslipidemia, two of eight (25%) had glaucoma. Among women with diabetes, 45 of 285 (15.80%) had glaucoma; among women with hypertension, 3 of 33 (9.09%) had glaucoma. No women with dyslipidemia had glaucoma.

Table 2 displays the results of the chi-square tests. The prevalence of PAC, NTG, OHT and SOAG were significantly related to older age ($p = 0.022$, 0.001, 0.001 and 0.021 respectively). Gender was significantly related to PAC ($p = 0.005$) and NTG ($p = 0.048$). Diabetes was significantly correlated with SOAG ($p = 0.041$) and dyslipidemia significantly related with SOAG ($p = 0.046$).

Table 2 Chi-square test results for participants glaucoma and glaucoma-related conditions

Characteristics	POAG	POAGS	PACG	PAC	NTG	OHT	SOAG
				Chi-Square (p-value)			
Age Groups	5.442	2.939	5.716 (0.126)	9.618	39.916	15.475	9.778
	(0.142)	(0.401)		(0.022)*	(0.000)***	(0.001)**	(0.021)*
Gender	2.133	0.049	0.836(0.361)	7.776	3.917	0.194	3.319
	(0.144)	(0.824)		(0.005)**	(0.048)*	(0.660)	(0.068)
Diabetes mellitus	0.054	0.202	0.520	0.037	0.028 (0.866)	1.310	4.164
	(0.816)	(0.653)	(0.471)	(0.847)		(0.252)	(0.041)*
Hypertension	0.061	0.354	1.080 (0.299)	0.848	0.021 (0.886)	1.765	1.247
	(0.805)	(0.552)		(0.357)		(0.184)	(0.264)
Dyslipidemia	0.122	0.166	0.197 (0.657)	0.730	0.425 (0.514)	0.322	3.988
	(0.738)	(0.733)		(0.393)		(0.570)	(0.046)*

Conclusion: * significant at 0.05 ** significant at 0.01 *** significant at 0.001(highly significance)
1. Age is significantly associated with PAC, NTG, OHT and SOAG
2. Gender is significantly associated with PAC, NTG
3. Diabetes is significantly associated with SOAG
4. Hypertension is not correlated with any type of glaucoma.
5. Dyslipidemia significantly correlated with SOAG

As shown in Table 3, the mean ages of subjects with NTG (68.82 ± 10.73 years), PACG (64.12 ± 10.66 years) and PAC (63.04 ± 10.95 years) were higher than those of the controls

(61.35 ± 11.93 years), while the mean ages of SOAG (58.36 ± 13.88) and OHT (55.77 ± 9.95 years) patients were lower than the non-glaucoma controls.

Table 3 Mean age of cases: glaucoma, glaucoma-related condition and no glaucoma, in RSU Eye Healthcare, 2015-2019

Characteristic (±SD)	No glaucoma	NTG	PACG	PAC	POAG	POAGS	SOAG	OHT
				Age in years Mean±SD				
Age at first Diagnosis	2,261 61.35±11.93	106 (68.82±10.73)	50 (64.12±10.66)	178 (63.04±10.95)	354 (62.78±11-97)	186 (59.47±11.22)	45 (58.36±13.88)	81 (55.77±9.95)
Male (1,544)	(922) 59.97±10.67	57 (67.35±10.69)	19 (61.53±9.58)	61 (60.64±10.02)	170 (62.51±12.48)	84 (59.18±11.90)	26 (60.27±14.40)	34 (55.68±9.64)
Female (1,924)	(1,201) 60.19±10.63	49 (70.53±10.63)	31 (65.71±11.11)	117 (64.29±11.24)	184 (63.03±11.51)	102 (59.72±10.68)	19 (55.74±13.06)	47 (55.83±10.27)
Diabetes mellitus	(526) 61.70±9.55	16 (69.25±11.50)	6 (66.00±8.15)	27 (64.11±11.06)	54 (66.41±13.80)	27 (60.63±12.23)	12 (56.00±14.85)	9 (51.22±9.35)
Hypertension	(70) 64.27±8.65	2 (80.00±1.41)	0	2	8 (59.50±6.36)	5 (63.13±11.40)	2 (58.20±11.37)	0 (46.00±4.24)
Dyslipidemia	(13) 62.54±7.29	0	0	0	1 (74.00)	1 (74.00)	1 (43.00)	0

Table 4 data also compares POAG and NTG in subjects with refractive errors and emmetropic subjects, illustrating that all degrees of myopia (mild, moderate and high), as well as mild and moderate hyperopia, were correlated with POAG and NTG. PACG would be expected to show the same correlations as POAG and NTG. There were no cases of POAG, NTG and PACG in individuals with a high degree of hyperopia, so a comparison with emmetropic subjects could not be made.

Table 4 Different types of glaucoma and correlation with refractive error

Ocular diseases with refractive error	Ocular diseases without refractive error	With refractive error (n)	Odds ratio	95% CI		P-value
POAG and NTG N=400	N=60	Mild myopia 167	.156	.132	.184	.000***
		Moderate myopia 31	.157	.108	.230	.000***
		High myopia 37	.138	.098	.195	.000**
		Mild hyperopia 119	.161	.132	.195	.000***
		Moderate hyperopia 46	.159	.116	.216	.000***
		High hyperopia 0	.000	0.000		.998
PACG N=49	1	Mild myopia 16	.013	.008	.021	.000***
		Moderate myopia 1	.004	.001	.031	.000***
		High myopia 1	.003	.000	.023	.000***
		Mild hyperopia 24	.029	.019	.043	.000***
		Moderate hyperopia 7	.021	.010	.045	.000***
		High hyperopia 0	.000	0.000		.998

POAG and NTG

1. The estimated odds in mild myopia are 6.41 (1/ 0.156) times higher compared with normal vision.

2. The estimated odds in moderate myopia are 6.37 (1/0.157) times higher compared with normal vision.

3. The estimated odds in high myopia are 7.25 (1/0.138) times higher compared with normal vision.

4. The estimated odds in mild hyperopia are 6.21 (1/0.161) times higher compared with normal vision.

5. The estimated odds in moderate hyperopia are 6.29 (1/0.159) times higher compared with normal vision.

6. No data on high hyperopia

PACG

1. The estimated odds in mild myopia are 76.92 (1/ 0.013) times higher compared with normal vision.

2. The estimated odds in moderate myopia are 250.00 (1/ 0.004) times higher compared with normal vision.

3. The estimated odds in high myopia are 333.00 (1/ 0.003) times higher compared with normal vision.

4. The estimated odds in mild hyperopia are 34.48 (1/ 0.029) times higher compared with normal vision.

5. The estimated odds in moderate hyperopia are 47.61 (1/ 0.021) times higher compared with normal vision.

6. No data on high hyperopia

5. Discussion
5.1 General

We find that when compared to emmetropic vision, all grades of myopia (mild, moderate, high) and all grades of hyperopia except high hyperopia were correlated with POAG, NTG and PACG (Table 4). Previous researchers in several countries including Singapore (Shen, Wong, Foster et al., 2008), the US (Marcus, de Vries, Montolio, & Jansonius, 2011) and China have often found a correlation between glaucoma and myopia, especially high myopia (Mitchell, Hourihan, Sandbach, & Wang, 1999; Wong et al., 2003; Xu, Wang, Wang, & Jonas, 2007; Perera et al., 2010). However, comparison of these studies is complicated because different criteria were used to diagnose glaucoma and different definitions (Australian or epidemiological) were used to classify refractive errors. More recent glaucoma studies relied more on visual field and optic nerve change than intraocular pressure (Jonas et al., 2017). Not all clinic-based glaucoma studies have examined its relationship with refractive error status (Jackson et al., 2014; Otabil, Tenkorang, Mac, & Otabil, 2013).

Our study noticed more myopia (36%) compared to the Fourth National population-based survey in Thailand in 2007, which found myopia (≤ -0.50 D) in 24% of the population (Jenchitr & Raiyawa ,2012). This study also found more normal-tension glaucoma compared to what has previously been found in Thailand (Bourne et. al., 2003). Additionally, 3.9% of glaucoma was found in 40-80-year-olds (Sothornwit, Jenchitr, Asawaphureekorn, & Rojanapongpun, 2019). Due to the age of our study population (60.1 ± 10.6 years), hyperopia (39.82%) was more common than myopia (33.27%) due to physiologic reduction of lens power because of hyperopic shift and to latent hyperopia appearance after loss accommodation (Iribarren et al., 2015).

We compared our results with those of several high-quality population-based studies from Singapore, Malaysia (Shen, Wong, Foster et al., 2008), the USA (Shen, Melles, Metlapally et al., 2016) and Australia (Mitchell, Smith, Attebo, & Healey, 1996). The mean age of the study population was younger than that of the population in the RSU study (58 and 60 years old, respectively), and therefore, the prevalence of POAG in myopic and hyperopic individuals was greater in the RSU study. In addition, because our study occurred in a university eye clinic, the number of glaucoma patients was greater than that found in population-based studies. More POAG were found among individuals with moderate to high myopia and mild to moderate hyperopia compared with subjects with similar degrees of refractive error in other studies.

Studies have found that NTG comprises 10% to 48% of all open-angle glaucoma cases in the United States, Europe and Scandinavia and up to 66% in the Japanese population (Chen, 2008). Japanese Americans have a fourfold higher rate of NTG compared to high tension glaucoma (Pekmezci et al., 2009). This form of glaucoma is more common in the elderly and in myopic individuals. Our study found NTG in 9.19% of myopes. The Rotterdam Eye study found a correlation of glaucoma with myopia (Czudowska et al., 2010), but after follow-up for 20 years, no correlation of glaucoma with hypertension and myopia (Springelkamp et al., 2017).

Myopia prevalence is increasing. In 2050, over 4.76 billion people will be expected to be myopic (50% of the world population) and 938 million of those are expected to have high myopia (10% of the world population; Holden et al., 2016). Optometrists and ophthalmologists must always be vigilant of the relationship between myopia and glaucoma and conduct primary eye-care screening at the time of the first prescription for presbyopia.

5.2 Strengths and limitations

A limitation of this study is its reliance upon clinical records. As noted above, the findings may therefore not be representative of the general Thai population.

A strength of this study is the large number of records available with sufficient information to diagnose glaucoma subtypes using standardized diagnostic criteria.

5.3 Recommendations

Future research should also include measurements of lens thickness (Mohamed-Noor, Bochmnn, Siddiqui et al., 2009) and anterior chamber depth to further assess the relationship between cataracts and angle-closure glaucoma (Xu, Cao, Wang, Chen, & Jonas, 2008). Research in younger age groups might also be useful, but care would need to be taken to control accommodation in younger subjects. The last recommendation is close follow up for ocular hypertension because it predicts the onset of primary open-angle glaucoma (Gordon, Beiser, Brandt et al, 2002; Coleman & Miglior, 2008).

6. Conclusion

In this study, we found that myopia and hyperopia were associated with all forms of open-angle and closed-angle glaucoma. Additionally, we found that secondary glaucoma was associated with diabetes and with dyslipidemia. Optometrists and other primary eye care workers conducting eye examinations must screen for eye diseases, particularly glaucoma, which is one of the leading causes of permanent blindness globally.

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