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Comparison of medical comorbidity between patients with primary angle-closure glaucoma and a control cohort: a population-based study from Taiwan

Hsin-Yi Chen,[1,2] Cheng-Li Lin[3]

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[1]Ophthalmology, China Medical University, Taichung, Taiwan
[2]Ophthalmology, Fu-Jen Catholic University Hospital, New Taipei, Taiwan
[3]Management Office for Health Data, China Medical University, Taichung, Taiwan

Correspondence to
Dr Hsin-Yi Chen;
hsin7850@url.com.tw

ABSTRACT

Objective To determine the prevalence and risk of systemic comorbidities in primary angle-closure glaucoma in Taiwan population.

Methods We included 3322 primary angle-closure glaucoma (PACG) subjects and randomly selected patients without PACG from the Taiwan National Health Insurance Research Database and frequency matched four of them (n=13 288) to each PACG patient, based on age and sex. The univariable and multivariable unconditional logistic regression models were used to estimate the effect of comorbidities on the risk of PACG as indicated by the OR with 95% CI.

Results The mean age of the PACG group was 65.2±12.7 years, and 61.1% of the patients were female. The risk of PACG was greater for patients with the comorbidities of hyperlipidaemia (ORs: 1.11), headaches (ORs: 1.13), liver diseases (ORs: 1.14), peptic ulcers (ORs: 1.10) and cataract (ORs: 3.80). For the male group, diabetes (ORs: 1.19), liver diseases (ORs: 1.29) and cataract (ORs: 4.30) were significantly associated with increasing PACG risk. For the female group, hyperlipidaemia (ORs: 1.13), headaches (ORs: 1.15), peptic ulcers (ORs: 1.14) and cataract (ORs: 3.54) were significantly associated with increasing PACG risk. For the age group of 64 years and younger, patients with comorbidity of hyperlipidaemia (ORs: 1.20), peptic ulcers (ORs: 1.21) and cataract (ORs: 5.91) were significantly associated with increasing PACG risk. For the age group of 65 years and older, patients with cataract were significantly associated with increasing PACG risk (ORs: 5.07).

Conclusions Clinicians should be aware of slightly increased PACG risk in the subjects with the medical comorbidities of hyperlipidaemia, headaches, liver diseases and peptic ulcers. However, cataract is the strongest risk factor of PACG.

Strengths and limitations of this study

- This is the first original study on the association between medical comorbidity and primary angle-closure glaucoma (PACG).
- A strength of this study is the large sample size.
- Clinicians should be aware of slightly increased PACG risk in the subjects with hyperlipidaemia, headaches, liver diseases and peptic ulcers.
- Cataract is the strongest risk factor of PACG in any age group and gender.
- This study has inherent limitations from the claims database, including miscoding and selection bias; the findings are thus not generalisable to all populations.

INTRODUCTION

Primary angle-closure glaucoma (PACG) is a leading cause of blindness worldwide; it is especially common in Asian countries.[1–3] A recent meta-analysis study shows that PACG affects approximately 0.75% of adult Asians, and this percentage doubles every decade; 60% of cases are in females.[4] The proposed mechanism of PACG is pupillary block, with anterior lens movement as a strong contributing factor, often due to ageing-induced cataract formation.[4 5] Risk factors for PACG are ageing, female gender, shallow anterior chamber and short axial length in hyperopic eye.[4 5] Contrary to primary open angle glaucoma (POAG)—which has been associated with systemic diseases, including cardiovascular, metabolic, neurodegenerative, psychological diseases and others[6–13] few studies have evaluated medical illness among PACG subjects. Age is the main factor contributing to the coexisting of systemic comorbidities and cataract formation. Therefore, it is quite meaningful to understand if age-related medical illness would be associated with PACG, which is also a very important issue in our population because of very high prevalence of this type of glaucoma in Taiwan.

Here, we use a nationwide dataset from Taiwan to determine the prevalence of some common medical comorbidities in the PACG population. We also study whether these comorbidities are associated with the increased risk of PACG compared with

controls. This is the first original study using a large claims database to evaluate this important topic.

MATERIALS AND METHODS

Patient and public involvement statement

This work is a retrospective longitudinal case–control study from a claims database. Patients were not involved in the recruitment or conduct of the study.

Data source

We conducted a nationwide population-based retrospective cohort study using data from the Longitudinal Health Insurance Database 2000 (LHID 2000). The LHID 2000 contains the enrolment and claims information of 1 million randomly sampled enrollees of the National Health Insurance (NHI) programme in 2000. The NHI programme provides mandatory universal health insurance to Taiwan's 23.75 million citizens and residents, with an enrolment rate of approximately 99%.[14]The LHID 2000 includes all ambulatory care, inpatient services, prescription drugs, traditional Chinese Medicine and dental services claims data. The study was approved by the Institutional Review Board of China Medical University and Hospital (CMUH-104-REC2-115). Diseases are coded according to the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM), 2001 edition.

Sampled participants

From the LHID 2000, we identified patients aged more than 20 years with a diagnosis of PACG (ICD-9-CM code 365.2) between January 1, 2005, and December 31, 2011 as the case group. The diagnosis of PACG was based on definitions agreed on by the World Glaucoma Association.[15] The date of diagnosis of PACG was defined as the index date. We excluded patients with a history of POAG (ICD-9-CM code 365.1) diagnosed before the index date. Secondary, juvenile, and congenital glaucoma were also excluded. For each PACG case, four insured beneficiaries with no history of glaucoma (ICD-9-CM code 365) were assigned to a non-PACG control group, frequency matched to the patients in the PACG case group according to age (every 5 years), sex and index year of PACG diagnosis; the same exclusion criteria used for the PACG case group were applied.

Common medical comorbidity

The comorbidities were hypertension (ICD-9-CM codes 401–405), ischaemic heart disease (ICD-9-CM codes 410–414), hyperlipidaemia (ICD-9-CM code 272), congestive heart failure (ICD-9-CM code 428), cardiac arrhythmias (ICD-9-CM codes 426 and 427), peripheral vascular disorders (ICD-9-CM codes 440.2, 440.3, 440.8, 440.9, 443, 444.22, 444.8, 447.8 and 447.9), stroke (ICD-9-CM codes 430–438), headaches (ICD-9-CM code 784.0), migraine (ICD-9-CM code 346), epilepsy (ICD-9-CM code 345), dementia (ICD-9-CM code 290, 294.1 and 331.0), rheumatoid arthritis (ICD-9-CM code 714), systemic lupus erythematosus (ICD-9-CM code 710.0), chronic obstructive pulmonary disease (ICD-9-CM codes 491, 492 and 496), asthma (ICD-9-CM code 493), pulmonary circulation disorders (ICD-9-CM codes 415–417), diabetes (ICD-9-CM code 250), hypothyroidism (ICD-9-CM codes 243 and 244), renal failure (ICD-9-CM codes 584–586), liver diseases (ICD-9-CM codes 570–573), peptic ulcers (ICD-9-CM codes 531–533), hepatitis B (ICD-9-CM codes V02.61, 070.20, 070.22, 070.30 and 070.32), tuberculosis (ICD-9-CM codes 011–018), deficiency anaemias (ICD-9-CM codes 280, and 281), depression (ICD-9-CM codes 296.2, 296.3, 300.4, and 311), psychosis (ICD-9-CM codes 295–299), metastatic cancer (ICD-9-CM codes 196–198) and solid tumour (ICD-9-CM codes 140–195).

Cataract (ICD-9-CM code 366) was also evaluated because of higher prevalence in the elderly population.

Statistical analysis

The baseline characteristics and comorbidities of the PACG case group and non-PACG control group were compared. X^2 test and t-test were used to evaluate the difference of categorical and continuous variables, respectively, between the two groups. Univariable and multivariable unconditional logistic regression models were used to estimate the effect of comorbidities on the risk of PACG as indicated by the OR with 95% CI. All analyses were performed using SAS V.9.4 (SAS Institute), and the significance level was set at 0.05 for the two-tailed tests.

RESULTS

A total of 3322 PACG cases met the study criteria, and 13 288 subjects were matched according to sex and age to form the control group (table 1). The PACG group comprised 61.1% women, and 57.6% were older than 65 years. The mean age was 65.2±12.7 years in the PACG group and 64.8±13.0 years in the control group. Compared with the controls, PACG patients have significantly higher prevalence of hypertension, ischaemic heart disease, hyperlipidaemia, cardiac arrhythmias, peripheral vascular disorders, headaches, chronic obstructive pulmonary disease, asthma, diabetes, renal failure, liver diseases, peptic ulcers, hepatitis B, depression, solid tumour and cataract ($p<0.05$).

The crude and adjusted ORs for the model were fitted to examine the association between medical comorbidities and the risk of PACG (table 2). Hyperlipidaemia increased the risk of PACG by 1.11-fold (95% CI: 1.01 to 1.21). Headaches increased the risk of PACG by 1.13-fold (95% CI: 1.04 to 1.23). Liver diseases inrcreased the risk of PACG by 1.14-fold (95% CI: 1.03 to 1.25). Peptic ulcers increased the risk of PACG by 1.10- fold (95% CI: 1.01 to 1.20). Cataract increased the risk of PACG by 3.80-fold (95% CI: 3.49 to 4.14).

For the male group, diabetes (ORs: 1.19, 95% CI: 1.00 to 1.40), liver diseases (ORs: 1.29, 95% CI: 1.11 to 1.50), and cataract (ORs: 4.30, 95% CI: 3.74 to 4.94)

Table 1 Demographic comparison between primary angle-closure glaucoma (PACG) cases and controls

	PACG cases n=3322		Controls n=13 288		
	n	(%)	n	(%)	P value
Sex					0.999
Female	2031	61.1	8124	61.1	
Male	5164	38.9	1291	38.9	
Age group (years)					0.999
20–49	398	12.0	1592	12.0	
50–64	1011	30.4	4044	30.4	
≥65	1913	57.6	7652	57.6	
Age (year), mean (SD)*	65.2 (12.7)		64.8 (13.0)		0.100
Comorbidity					
Hypertension	2025	60.6	6896	51.9	<0.001
Ischaemic heart disease	1097	33.0	3561	26.8	<0.001
Hyperlipidaemia	1389	41.8	4399	33.1	<0.001
Congestive heart failure	213	6.41	849	6.39	0.962
Cardiac arrhythmias	540	16.3	1826	13.7	<0.001
Peripheral vascular disorders	201	6.05	571	4.30	<0.001
Stroke	246	7.41	994	7.48	0.883
Headaches	1407	42.4	4772	35.9	<0.001
Migraine	125	3.76	456	3.43	0.353
Epilepsy	30	0.90	144	1.08	0.360
Dementia	110	3.31	448	3.37	0.863
Rheumatoid arthritis	11	0.33	45	0.34	0.957
Systemic lupus erythematosus	3	0.09	8	0.06	0.546
Chronic obstructive pulmonary disease	675	20.3	2343	17.6	<0.001
Asthma	418	12.6	1455	11.0	0.008
Pulmonary circulation disorders	26	0.78	85	0.64	0.366
Diabetes	710	21.4	2148	16.2	<0.001
Hypothyroidism	36	1.08	110	0.83	0.158
Renal failure	448	13.5	1435	10.8	<0.001
Liver diseases	898	27.0	2775	20.9	<0.001
Peptic ulcers	1409	42.4	4503	33.9	<0.001
Hepatitis B	182	5.48	610	4.59	0.032
Tuberculosis	86	2.59	294	2.21	0.194
Deficiency anaemia	114	3.43	381	2.87	0.087
Depression	328	9.87	922	6.94	<0.001
Psychosis	153	4.61	518	3.90	0.064
Metastatic cancer	1	0.03	2	0.02	0.564
Solid tumour	190	5.72	630	4.74	0.020
Cataract	2088	62.9	4077	30.7	<0.001

Data are presented as the number of subjects in each group, with percentages given in parentheses.
χ^2 test; *t-test.

Table 2 Factors associated with risk of primary angle-closure glaucoma

	Crude	Adjusted†
Variable	OR (95% CI)	OR (95% CI)
Comorbidity		
Hypertension	1.45 (1.34 to 1.56)***	0.97 (0.88 to 1.07)
Ischaemic heart disease	1.35 (1.24 to 1.46)***	0.92 (0.83 to 1.01)
Hyperlipidaemia	1.45 (1.34 to 1.57)***	1.11 (1.01 to 1.21)*
Congestive heart failure	1.00 (0.86 to 1.17)	–
Cardiac arrhythmias	1.22 (1.10 to 1.35)***	0.91 (0.81 to 1.02)
Peripheral vascular disorders	1.44 (1.22 to 1.69)***	1.02 (0.86 to 1.21)
Stroke	0.98 (0.86 to 1.14)	–
Headaches	1.31 (1.21 to 1.42)***	1.13 (1.04 to 1.23)***
Migraine	1.10 (0.90 to 1.35)	–
Epilepsy	0.83 (0.56 to 1.24)	–
Dementia	0.98 (0.79 to 1.21)	–
Rheumatoid arthritis	0.98 (0.51 to 1.89)	–
Systemic lupus erythematosus	1.50 (0.40 to 5.66)	–
Chronic obstructive pulmonary disease	1.19 (1.08 to 1.31)***	0.88 (0.79 to 1.00)
Asthma	1.17 (1.04 to 1.32)***	0.98 (0.86 to 1.11)
Pulmonary circulation disorders	1.23 (0.79 to 1.90)	–
Diabetes	1.41 (1.28 to 1.55)***	1.03 (0.93 to 1.15)
Hypothyroidism	1.31 (0.90 to 1.92)	–
Renal failure	1.29 (1.15 to 1.44)***	0.93 (0.82 to 1.05)
Liver diseases	1.40 (1.29 to 1.53)***	1.14 (1.03 to 1.25)*
Peptic ulcers	1.44 (1.33 to 1.55)***	1.10 (1.01 to 1.20)*
Hepatitis B	1.21 (1.02 to 1.43)*	1.09 (0.91 to 1.31)
Tuberculosis	1.18 (0.92 to 1.50)	–
Deficiency anaemia	1.20 (0.97 to 1.49)	–
Depression	1.47 (1.29 to 1.68)***	1.12 (0.98 to 1.29)
Psychosis	1.19 (0.99 to 1.43)	–
Metastatic cancer	2.01 (0.18 to 22.1)	–
Solid tumour	1.22 (1.03 to 1.44)*	1.01 (0.85 to 1.20)
Cataract	3.82 (3.53 to 4.14)***	3.80 (3.49 to 4.14)***

*p<0.05; **p<0.01; ***p<0.001.
†Covariables which were significantly associated with risk of PACG in univariable unconditional logistic regression model were further analysed by multivariable unconditional logistic regression model.

were significantly associated with increasing PACG risk (table 3). For the female group, hyperlipidaemia (ORs: 1.13, 95% CI: 1.00 to 1.26), headaches (ORs: 1.15, 95% CI: 1.04 to 1.28), peptic ulcers (ORs: 1.14, 95% CI: 1.02 to 1.28) and cataract (ORs: 3.54, 95% CI: 3.18 to 3.95) were significantly associated with increasing PACG risk.

For the age group of 64 years and younger, patients with comorbidity of hyperlipidaemia (ORs: 1.20, 95% CI: 1.03 to 1.40), peptic ulcers (ORs: 1.21, 95% CI: 1.05 to 1.40), and cataract (ORs: 5.91, 95% CI: 5.07 to 6.90) were significantly associated with increasing PACG risk (table 4). For the age group of 65 years and older, patients with cataract were significantly associated with increasing PACG risk (ORs: 5.07, 95% CI: 4.46 to 5.77).

DISCUSSION

Among the 3322 PACG patients, 41.8% had hyperlipidaemia, 42.4% had headache and peptic ulcer and 62.9% had cataract. The risk of PACG was greater for patients with the comorbidities of hyperlipidaemia, headaches, liver diseases, peptic ulcers, and cataract. For the male group, diabetes, liver diseases and cataract were significantly associated with increasing PACG risk. For the

Table 3 Factors affecting the risk of primary angle-closure glaucoma according to sex

	Male		Female	
	Crude	Adjusted†	Crude	Adjusted†
Variable	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Comorbidity				
Hypertension	1.60 (1.41 to 1.81)***	1.01 (0.87 to 1.18)	1.36 (1.23 to 1.50)***	0.94 (0.83 to 1.06)
Ischaemic heart disease	1.43 (1.25 to 1.63)***	0.92 (0.78 to 1.08)	1.30 (1.17 to 1.44)***	0.90 (0.79 to 1.02)
Hyperlipidaemia	1.54 (1.35 to 1.75)***	1.12 (0.96 to 1.30)	1.41 (1.28 to 1.56)***	1.13 (1.00, 1.26)*
Congestive heart failure	1.15 (0.91 to 1.46)	–	0.91 (0.74 to 1.12)	–
Cardiac arrhythmias	1.24 (1.05 to 1.48)***	0.86 (0.71 to 1.05)	1.20 (1.06 to 1.37)***	0.93 (0.80 to 1.07)
Peripheral vascular disorders	1.52 (1.17 to 1.98)***	0.97 (0.73 to 1.29)	1.38 (1.12 to 1.71)***	1.04 (0.84 to 1.31)
Stroke	1.10 (0.89 to 1.36)	–	0.90 (0.74 to 1.10)	–
Headaches	1.35 (1.19 to 1.55)***	1.15 (1.00 to 1.33)	1.30 (1.18 to 1.44)***	1.15 (1.04, 1.28)**
Migraine	1.09 (0.70 to 1.70)	–	1.10 (0.88 to 1.39)	–
Epilepsy	0.91 (0.50 to 1.67)	–	0.78 (0.46 to 1.31)	–
Dementia	1.04 (0.74 to 1.45)	–	0.95 (0.72 to 1.25)	–
Rheumatoid arthritis	2.01 (0.37 to 11.0)	–	0.88 (0.43 to 1.81)	–
Systemic lupus erythematosus	4.00 (0.25 to 64.0)	–	1.15 (0.24 to 5.52)	–
Chronic obstructive pulmonary disease	1.34 (1.17 to 1.54)***	0.89 (0.75 to 1.05)	1.07 (0.94 to 1.23)	–
Asthma	1.30 (1.08 to 1.56)***	0.99 (0.80 to 1.23)	1.10 (0.95 to 1.28)	–
Pulmonary circulation disorders	1.07 (0.49 to 2.34)	–	1.31 (0.77 to 2.24)	–
Diabetes	1.67 (1.44 to 1.94)***	1.19 (1.00 to 1.40)*	1.26 (1.11 to 1.42)***	0.93 (0.81 to 1.07)
Hypothyroidism	1.18 (0.43 to 3.20)	–	1.34 (0.89 to 2. 01)	–
Renal failure	1.46 (1.23 to 1.73)***	0.96 (0.80 to 1.16)	1.17 (1.00 to 1.36)*	0.87 (0.74 to 1.03)
Liver diseases	1.57 (1.37 to 1.80)***	1.29 (1.11 to 1.50)**	1.30 (1.16 to 1.46)***	1.05 (0.92 to 1.19)
Peptic ulcers	1.40 (1.24 to 1.59)***	1.01 (0.87 to 1.16)	1.46 (1.32 to 1.61)***	1.14 (1.02, 1.28)*
Hepatitis B	1.25 (0.97 to 1.61)	–	1.17 (0.93 to 1.47)	–
Tuberculosis	1.29 (0.95 to 1.75)	–	1.02 (0.68 to 1.52)	–
Deficiency anaemia	1.48 (0.99 to 2.20)	–	1.12 (0.87 to 1.44)	–
Depression	1.67 (1.31 to 2.13)***	1.20 (0.93 to 1.57)	1.40 (1.20 to 1.64)***	1.11 (0.94 to 1.31)
Psychosis	1.13 (0.81 to 1.59)	–	1.22 (0.98 to 1.52)	–
Metastatic cancer	–	–	–	–
Solid tumour	1.23 (0.93 to 1.61)	–	1.22 (0.98 to 1.50)	–
Cataract	4.37 (3.84 to 4.96)***	4.30 (3.74 to 4.94)***	3.54 (3.20 to 3.92)***	3.54 (3.18 to 3.95)***

*p<0.05; **p<0.01; ****p<0.001.
†Covariables which were significantly associated with risk of PACG in univariable unconditional logistic regression model were further analysed by multivariable unconditional logistic regression model.

female group, hyperlipidaemia, headaches, peptic ulcers and cataract were significantly associated with increasing PACG risk. For both the genders, cataract was the same and strongest risk factor for PACG development (ORs: 4.30 for the male group; ORs: 3.54 for the female group).

Regarding the effect of age on the risk of PACG, we subclassified the study groups into two. Interesting results were obtained; patients with comorbidity of hyperlipidaemia, peptic ulcers and cataract were associated with increasing PACG risk in the age group of 64 years and younger. However, for the age group of 65 years and older, cataract was the only factor for the increased risk of PACG. Cataract was the same and strongest risk factor for PACG onset for both the age groups (ORs: 5.91 for the age group younger than 65 years; ORs: 5.07 for the age group older than 65 years).

Our study is the first one that discussed the medical comorbidity in a large PACG cohort using large claims database. Potential explanations about the strong relationship between some medical illness and the risk of PACG should be mentioned as below.

Table 4 Factors affecting the risk of primary angle-closure glaucoma according to the age

	Age ≤64		Age ≥65	
	Crude	Adjusted†	Crude	Adjusted†
Variable	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Comorbidity				
Hypertension	1.77 (1.57 to 2.00)***	1.15 (0.99 to 1.34)	1.35 (1.20 to 1.51)***	1.10 (0.97 to 1.25)
Ischaemic heart disease	1.79 (1.54 to 2.08)***	1.00 (0.83 to 1.21)	1.23 (0.11 to 1.36)***	0.95 (0.84 to 1.07)
Hyperlipidaemia	1.81 (1.60 to 2.06)***	1.20 (1.03 to 1.40)*	1.28 (1.15 to 1.41)***	1.04 (0.92 to 1.16)
Congestive heart failure	1.75 (1.24 to 2.48)***	0.96 (0.64 to 1.44)	0.89 (0.74 to 1.06)	–
Cardiac arrhythmias	1.49 (1.22 to 1.83)***	1.01 (0.80 to 1.28)	1.14 (1.01 to 1.29)*	0.92 (0.80 to 1.06)
Peripheral vascular disorders	1.65 (1.14 to 2.40)***	0.84 (0.55 to 1.28)	1.40 (1.16 to 1.68)***	1.13 (0.93 to 1.38)
Stroke	1.40 (0.99 to 1.96)	–	0.92 (0.78 to 1.08)	–
Headaches	1.48 (1.31 to 1.67)***	1.14 (1.00 to 1.30)	1.20 (1.09 to 1.33)***	1.04 (0.93 to 1.16)
Migraine	1.13 (0.83 to 1.52)	–	1.08 (0.83 to 1.42)	–
Epilepsy	1.17 (0.61 to 2.24)	–	0.70 (0.42 to 1.15)	–
Dementia	2.46 (1.16 to 5.21)***	1.31 (0.57 to 3.05)	0.92 (0.73 to 1.15)	–
Rheumatoid arthritis	1.26 (0.50 to 3.17)	–	0.77 (0.30 to 2.00)	–
Systemic lupus erythematosus	2.01 (0.18 to 22.1)	–	1.33 (0.27 to 6.61)	–
Chronic obstructive pulmonary disease	1.60 (1.33 to 1.93)***	1.08 (0.87 to 1.34)	1.09 (0.97 to 1.22)	–
Asthma	1.42 (1.15 to 1.76)***	1.00 (0.78 to 1.28)	1.08 (0.94 to 1.25)	–
Pulmonary circulation disorders	1.72 (0.66 to 4.48)	–	1.13 (0.69 to 1.86)	–
Diabetes	1.92 (1.63 to 2.25)***	1.08 (0.89 to 1.31)	1.21 (1.08 to 1.37)**	0.96 (0.84 to 1.09)
Hypothyroidism	1.28 (0.71 to 2.30)	–	1.34 (0.81 to 2.19)	–
Renal failure	1.82 (1.48 to 2.24)***	1.08 (0.85 to 1.37)	1.13 (0.99 to 1.30)	–
Liver diseases	1.64 (1.43 to 1.87)***	1.12 (0.96 to 1.31)	1.26 (1.13 to 1.42)***	1.02 (0.90 to 1.16)
Peptic ulcers	1.70 (1.50 to 1.92)***	1.21 (1.05 to 1.40)**	1.32 (1.19 to 1.45)***	1.06 (0.95 to 1.19)
Hepatitis B	1.06 (0.83 to 1.35)	–	1.37 (1.08 to 1.73)***	1.20 (0.93 to 1.54)
Tuberculosis	1.08 (0.64 to 1.82)	–	1.21 (0.92 to 1.59)	–
Deficiency anaemia	1.36 (0.95 to 1.92)	–	1.13 (0.86 to 1.47)	–
Depression	1.78 (1.45 to 2.20)***	1.18 (0.93 to 1.50)	1.31 (1.10 to 1.55)**	1.01 (0.85 to 1.21)
Psychosis	1.27 (0.95 to 1.69)	–	1.14 (0.90 to 1.45)	–
Metastatic cancer	–	–	–	–
Solid tumour	1.16 (0.83 to 1.60)	–	1.25 (1.02 to 1.51)*	1.15 (0.94 to 1.41)
Cataract	6.95 (6.00 to 8.05)***	5.91 (5.07 to 6.90)***	5.18 (4.56 to 5.87)***	5.07 (4.46 to 5.77)***

*p<0.05; **p<0.01; ****p<0.001.
†Covariables which were significantly associated with risk of PACG in univariable unconditional logistic regression model were further analysed by multivariable unconditional logistic regression model.

Pathogenetic mechanisms of PACG and association between cataract and PACG

Our study reveals that cataract is the strongest risk factor for PACG in any age group and gender compared to other medical comorbidity. PACG has its characteristic anatomy features and unique pathological process, including a crowded anterior segment and narrow anterior chamber angle.[15] The lens is considered to play a crucial role in the pathogenesis of PACG either because of an increase in its thickness or a more anterior position resulting in angle crowding and a greater predisposition to pupillary block.[5 6 15 16] Furthermore, the lens thickness increases with age and makes the narrow anterior chamber angle even more crowded, which might be why most PACG occurs in patients older than 40 years.[15 16] Our study result supports that ocular anatomical factor plays a more important role in the pathogenesis of PACG than any other medical comorbidities in Taiwan Chinese population.

Association between hyperlipidaemia and diabetes and PACG

In one Korean epidemiological study, hypercholesterolemia, hypertension and diabetes mellitus were independent risk factors for the development of any cataract.[17] Moreover, in one study, the authors demonstrated that metabolic syndrome and its components are associated with age-related cataract only among Korean women.[18] We believe that the potential reasons for diabetes and hyperlipidaemia in the risk of PACG from our result could be attributed to the increased risk of cataract. Further, longitudinal observational study is needed to address this issue.

Association between liver disease and PACG

One recent study from Taiwan reported that hepatitis C infection, even without the complication of cirrhosis, is associated with an increased risk of cataract.[19] Another study from Korean reported that hepatitis B and hepatitis C infection were significantly associated with cataract.[20] The strong association between liver disease and the risk of PACG might increase the risk of cataract in liver disease patients. However, further study is needed to elucidate this interesting result.

Association between headache and PACG

PACG patients complain of headache caused by increased intraocular pressure.[21 22] PACG patients seek medical help due to headache before the diagnosis of PACG. Our results indicate that headache is associated with higher risk for PACG. Headache may be a symptom of PACG missed by the physician. Therefore, clinicians should consider the possibility of PACG in patients with headache.

Association between peptic ulcers and PACG

No previous study has reported the presence or absence of an association between peptic ulcers and PACG. We speculate that Histamine 2 receptor antagonist that was widely used in peptic ulcer treatment might induce or precipitate PACG.[23] Further longitudinal study is mandatory in this interesting topic.

Despite these promising results, our study had certain limitations. First, glaucoma and medical comorbidity were defined entirely on the basis of claims data (ICD-9-CM codes assigned by clinicians).[21] This approach is less accurate than diagnosing personally through a standardised procedure.[21] The second limitation is selection bias.[21] Because the NHI database only comprises data of patients who have received treatment, patients who have received no treatment for glaucoma or any of these medial disease might have been recruited in the comparison cohort. Third, despite the large sample, the study cohort comprised Taiwanese patients. Therefore, these findings cannot be generalised to other populations. Nevertheless, our study has the following strengths. First, the strength of the database is excellent because of the large sample randomization.[21] We could follow patient cases over time to assess the relationship between medical illness and the subsequent onset of PACG. Second, the database includes data of people with diverse sociodemographic profiles, unlike some smaller studies that recruited patients from specific regions and thus lack in representativeness.

In conclusion, our population-based study using the NHIRD revealed that the PACG risk is strongest in cataract patients and is slightly higher in patients with medical comorbidities of hyperlipidaemia, headaches, liver diseases, and peptic ulcers. Clinicians should be aware of these findings when encountering patients with these diseases.

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