Heliyon 10 (2024) e34090

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon

Research article

Acute primary angle closure concurrent with coronavirus disease 2019 recurrence in Northern China: A retrospective multi-centre study

Ye Zhang [a,1], Su Jie Fan [b,1], Xiao Jing Pan [c,1], Zhi Hong Zhang [b], Qing Shu Ge [c], Jin Wang [a,d], Yue Wang [a,d], Ming Guang He [e], Ning Li Wang [a,d,*]

[a] *Beijing Tongren Eye Center, Beijing Key Laboratory of Ophthalmology and Visual Science, Beijing Tongren Hospital, Capital Medical University, Beijing, China*

[b] *Handan City Eye Hospital, Handan, China*

[c] *Shandong Provincial Key Laboratory of Ophthalmology-State Key Laboratory Cultivation Base, Qingdao Eye Hospital of Shandong First Medical University Shandong Eye Institute, Qingdao, China*

[d] *Beijing Institute of Ophthalmology, Beijing, China*

[e] *Centre for Eye and Vision Research (CEVR), The Hong Kong Polytechnic University, Kowloon, Hong Kong SAR, China*

ARTICLE INFO

Keywords:
Acute angle closure
Concurrent increase
Coronavirus disease 2019

ABSTRACT

Aims and objectives: During the new coronavirus disease 2019 (COVID-19) outbreak period, there was increasing presentation in the number of patients with acute primary angle closure (APAC). This study aimed to report the occurrence of APAC during the COVID-19 post-restriction period and investigate the related characteristics of these patients with APAC.

Methods: This retrospective, multi-center study included consecutive patients seeking APAC treatment at two eye centers in China from December 7, 2022 to January 13, 2023 (post-restriction period) and from December 7, 2021 to January 13, 2022 (control period). Electronic medical records were reviewed, and ocular data of the affected eye(s) were analyzed for patients with unilateral or bilateral APAC. Information including COVID-19 related symptoms, medications used for COVID-19 infection, and living habits and emotions related to the COVID-19 outbreak during the post restriction period were collected using a questionnaire.

Results: Overall, 189 (219 APAC eyes) and 51 (54 APAC eyes) patients with APAC were identified during the post-restriction and control periods, respectively. The patients identified during the post-restriction period were younger ($P = 0.043$) and had a longer duration from symptoms to treatment ($P = 0.039$), shorter axial length ($P = 0.002$), larger pupil diameter ($P = 0.004$), larger vertical cup disc ratio ($P = 0.004$), poorer mean deviation values ($P = 0.003$), and more glaucomatous optic neuropathy diagnoses ($P = 0.032$) compared with the patients with APAC identified during the control period. Among 151 included patients with APAC who completed the questionnaires, 130 patients with APAC were diagnosed with concurrent COVID-19 infection, of which 54 (41.5 %) had coughing and/or vomiting as the main symptoms. Of these, 89.2 % spent 0 h per day on outdoor activity; 44.6 % drank more water than usual, with 14.6 % drinking more

* Corresponding author. Beijing Institute of Ophthalmology, Beijing Tongren Eye Center, Beijing Tongren Hospital, Capital Medical University, Beijing Key Laboratory of Ophthalmology and Visual Sciences, No. 1 Dong Jiao Min Xiang Street, Dongcheng District, Beijing, 100730, China.
E-mail address: wningli@vip.163.com (N.L. Wang).

[1] These three authors contributed equally to this work.

https://doi.org/10.1016/j.heliyon.2024.e34090
Received 7 October 2023; Received in revised form 27 June 2024; Accepted 3 July 2024
Available online 4 July 2024

than twice the amount of water than usual; 91.5 % used antipyretics; and 20.0 % had mood swings, including anxiety, depression, and tension, during the concurrent COVID-19 infection.
Conclusion: In our study, a significant increase in the number of patients presenting with APAC with certain characteristics was observed during the COVID-19 post-restriction period. And whether COVID-19 symptoms, such as coughing and vomiting, and behavioral and psychological changes caused by COVID-19 infection contributing to the concurrence of APAC and COVID-19 recurrence require further investigation.

1. Introduction

The coronavirus disease 2019 (COVID-19) is caused by the severe acute respiratory syndrome coronavirus-2 spread by human-to-human transmission [1,2]. COVID-19 has remained a global pandemic since its outbreak in December 2019 [1–3]. After experiencing the large-scale epidemic in February 2020, China entered a normalization stage of prevention and control from May 2020 [4]. In response to the COVID-19 pandemic, the Chinese government implemented a strategy called "Dynamic Zero-COVID" from August 2021 [5], and almost three years after the first COVID-19 case was reported, China has taken decisive steps toward "living with the virus." On December 7, 2022, the Chinese Government issued the New 10 Epidemic Prevention Policy, removing requirements such as mandatory centralized quarantine, compulsory testing, and sweeping lockdowns, and announced that China's Dynamic Zero-COVID policy had officially moved towards the reopening of the country [6,7].

With the rapid spread of the highly transmissible Omicron variant, a new COVID-19 pandemic in China was inevitable. By January 13, 2023, 97,080,949 confirmed cases and 93,496 deaths were reported in China [8].

During the new COVID-19 outbreak from December 7, 2022, many ophthalmologists in China noticed an increasing number of patients presenting with acute primary angle closure (APAC) [9,10]. And several case reports have demonstrated the development of APAC concurrently with COVID-19 [11–16]. APAC, a subtype of primary angle closure disease, presents with sudden obstruction of the anterior chamber angle, resulting in a rapid rise in intraocular pressure (IOP) to high levels, which is considered an ocular emergency and requires immediate intervention and associated with a high rate of blindness, especially in East Asia [17–19]. A narrow anterior chamber angle, advanced age, female sex, and Asian ethnic background are considered risk factors for APAC [18]. Moreover, associations between APAC attacks and stressful life changes; Valsalva maneuvers, such as forceful coughing, heavy lifting, and vomiting; systemic infection; and certain drugs have been reported [18,20–23]. Some of these precipitating factors attributing to APAC attacks may have existed concurrently with the COVID-19 pandemic since December 7, 2022.

This study aimed to investigate the occurrence of APAC cases in China during the new COVID-19 pandemic, based on a multi-center survey, and to further explore the characteristics of these APAC cases and possible risk factors.

2. Materials and methods

2.1. Study population

This observational, retrospective, multi-center study based on electronic medical records included patients with APAC visiting glaucoma clinics (out-patient department or emergency department) for treatment at Handan City Eye Hospital (HCEH; a second-class grade-A specialized hospital in Hebei Province, Northern China) and Qingdao Eye Hospital (QEH; a third-class grade-A specialized hospital in Shandong Province, Northern China). These two eye centers are leading eye hospitals in their respective cities located in Northern China. They serve as primary ophthalmic care providers for their local communities, with the vast majority of their patients being residents of the surrounding areas rather than migrant populations. Furthermore, these two centers maintain comprehensive electronic medical record systems and standardized clinical examination protocols.

Consecutive APAC cases encountered during the new COVID-19 outbreak period from December 7, 2022 to January 13, 2023 (38 days) (post-restriction period) and consecutive APAC cases encountered during the Dynamic Zero-COVID period from December 7, 2021 to January 13, 2022 (38 days) (control period) were included.

The inclusion criteria were age $\geq$40 years and a diagnosis of APAC during the abovementioned periods. APAC was defined according to the following criteria: (1) the presence of two or more of the following symptoms: ocular or periocular pain, nausea and/or vomiting, or an antecedent history of intermittent blurring of vision with halos; (2) presenting IOP of $>$21 mmHg; (3) the presence of at least three of the following signs: conjunctival injection, corneal edema, a mid-dilated unreactive pupil in affected eyes, or a shallow anterior chamber in both eyes; and (4) the presence of an occluded angle in the affected eye that could be verified by gonioscopy or ultrasound biomicroscopy [24]. The exclusion criteria were presentation of secondary angle closure, such as subluxation lens-induced glaucoma, neovascular glaucoma, or uveitic glaucoma, or a history of intraocular surgeries or hospitalization because of glaucoma. The affected eye or both eyes were selected for ocular data collection for patients with unilateral or bilateral APAC, respectively.

2.2. Procedures

Demographic characteristics and history, including ocular diseases, medications, laser treatment/surgeries, and trauma and systemic diseases and medications, were collected from patients with APAC belonging to the post-restriction and control period groups.

Ocular data, including IOP measured by a rebound tonometer (SW-500, Tianjin Suowei Electronic Technology Co, Tianjin, China [HCEH] and Icare PRO-TA03, Icare Finland Oy, Helsinki, Finland [QEH]), presenting visual acuity (PVA) and slit-lamp examinations at diagnosis and after initial treatment, best corrected distance visual acuity (BCVA), automated refraction (Topcon RM-8900, Topcon Co, Tokyo, Japan [HCEH] and NIDEK AOS-3000, NIDEK Co, Gamagori, Japan [QEH]), ocular biometry (IOL Master 500 and 700, Carl Zeiss Meditec, Jena, Germany [HCEH and QEH]), corneal endothelial cell count (Topcon SP-3000P [HCEH] and Topcon NSP-9000II [QEH], both Topcon Co), ultrasound biomicroscopy (SW-3200L, Tianjin Suowei Electronic Technology Co [HCEH and QEH]), fundus photography (KOWA Nonmyd WX, KOWA Co., Nagoya, Japan [HCEH] and Optomap, Daytona, OPTOS Co., Scotland, UK [QEH]), and visual field tests (Humphrey 750i Visual Field Analyzer [HCEH] and HFA MODEL 860 [QEH], both Carl Zeiss Meditec) after initial treatment, were also collected from the two periods. According to previous studies, the results of IOL Master 500 and 700 in measuring average keratometry (AK), central corneal thickness (CCT), central anterior chamber depth (ACD), lens thickness (LT), and axial length (AL) are of high agreement [25,26].

Data, mainly focused on the date and time from symptoms to treatment (TST) of the APAC attack, COVID-19-related symptoms including fever, headache, coughing, nausea, vomiting fatigue, dyspnea, myalgia, chest pain, dyspnea, diarrhea and et al., medications used for COVID-19 infection including ibuprofen, acetaminophen, cough syrup, anti-histamines, hypnotics and et al., outdoor activity time, changes in water drinking habits, and emotions related to the COVID-19 outbreak that may have played a role in the APAC attack during the post-restriction period including anxiety, depression, tension and et al., were collected from patients using a questionnaire.

2.3. Definitions and data collection

The spherical equivalent (SE) was calculated as sphere + 0.5 × cylinder. All the fundus photographs were evaluated by a glaucoma specialist (Y.Z.). Glaucomatous optic neuropathy (GON) was defined as the loss of the neuroretinal rim with a vertical cup-to-disc ratio (VCDR) of ≥0.6 and/or notching and/or visible retinal nerve fiber layer defect attributable to glaucoma [27,28]. Blindness of the affected eye was defined as <3/60 Snellen visual acuity, which is in accordance with the definition by the World Health Organization (WHO) [29].

The numbers of monocular and binocular eyes being affected; ratios of patients with APAC among patients at the glaucoma departments in the two hospitals; TST, PVA, IOP, and rate of blindness at diagnosis; PVA, BCVA, SE, IOP, and rate of blindness after initial interventions; corneal endothelial cell count; ocular biometry (using IOL Master), including average keratometry (AK), central corneal thickness (CCT), central anterior chamber depth (ACD), lens thickness (LT), axial length (AL), pupil diameter (PD), and VCDR; and the results of visual field tests, including mean deviation (MD), pattern standard deviation (PSD), and visual field index (VFI), during the post-restriction and control periods were collected and compared between patients from the two periods. The numbers and ratios of different initial interventions for APAC eyes from the two periods were also collected.

2.4. Statistical analysis

All statistical analyses were performed using the SPSS statistical software (version 25.0; IBM Corp., Armonk, NY, USA). The Shapiro–Wilk test was used to evaluate the normality of continuous variables. Descriptive results were presented as the mean and standard deviation for normally distributed continuous variables. The median value and interquartile range were used for non-normally distributed continuous variables.

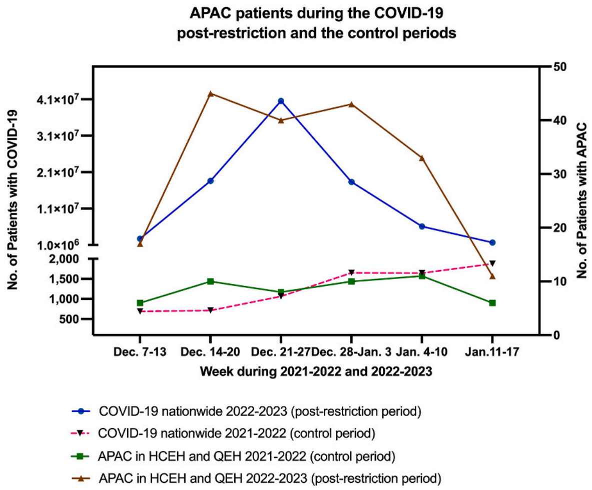

Fig. 1. Numbers of patients with APAC at HCEH and QEH during the post-restriction and control periods, relative to the number of COVID-19 patients nationwide during the two periods. APAC, acute primary angle closure; COVID-19, coronavirus disease 2019; HCEH, Handan City Eye Hospital; QEH, Qingdao Eye Hospital.

The *t*-test and the Mann–Whitney *U* test were used to analyze the differences between the two periods for normally distributed and non-normally distributed continuous variables, respectively. The chi-square or Fisher's exact test were used for categorical variables to detect differences between the two periods. For all tests, *P*-values <0.05 were considered statistically significant.

Univariate and multivariate logistic regression analyses were conducted to determine the factors associated with the occurrence of APAC during the COVID-19 post-restriction period. Variables with *P* values < 0.05 in the univariate analysis were then added to the multivariate analysis, and variables with *P* values greater than 0.05 were excluded from the final multivariate model. And a variance inflation factor (VIF) < 2 was an acceptable degree of multicollinearity in our study.

3. Results

3.1. Increased APAC presentations during the COVID-19 post-restriction period

Overall, there were 189 patients with APAC (219 APAC eyes) aged 67.6 (62.8, 72.0) years with 20.1 % males during the post-restriction period and 51 patients with APAC (54 APAC eyes) aged 69.0 (64.2, 76.0) years with 21.6 % males during the control period. There was an increase in the number of patients with APAC during the post-restriction period when compared with the control period. The numbers of APAC cases at HCEH and QEH during the post-restriction and control periods relative to the number of COVID-19 cases nationwide during the post-restriction period are shown in Fig. 1. Characteristics of patients with APAC included from HCEH and QEH respectively during two periods are summarized in Supplementary Table 1.

The ratio of patients with APAC among the overall patients of the glaucoma departments at the two hospitals during the post-restriction period was higher than that during the control period (189/321 [58.9 %] vs. 51/331 [15.4 %]). This difference was statistically significant (P < 0.001).

3.2. Characteristics of patients with APAC during the post-restriction period

Patients with APAC during the post-restriction period were younger (*P* = 0.043) and had a longer TST (*P* = 0.039) compared with those during the control period. The ratio of bilateral involvement was higher in patients with APAC during the post-restriction period than that during the control period (15.9 % vs. 5.9 %), but there was no significant difference (*P* = 0.066). There were no significant differences in sex composition and systemic diseases, including hypertension and diabetes, between the patients with APAC during the two periods (Table 1). Initial PVA; rate of blindness and IOP at diagnosis; and PVA, BCVA, rate of blindness, IOP, and SE after initial interventions were similar in patients with APAC during the two periods (Table 2).

Comparisons of ocular parameters assessed after initial interventions between APAC eyes during the post-restriction and control periods showed that the former had shorter AL (*P* = 0.002), larger PD (*P* = 0.004), larger VCDR (*P* = 0.004), and poorer MD (*P* = 0.003) and VFI (*P* = 0.007) values compared with the latter. Fundus photographs of the 210 included APAC eyes were readable. The proportion of GON in APAC eyes during the post-restriction period (49.7 %) was higher than that during the control period (30.8 %) This difference was statistically significant (*P* = 0.032). No significant differences were found in corneal endothelial cell count, AK, CCT, central ACD, LT, and pattern standard deviation values between APAC eyes during the two periods (*P* > 0.05). (Table 3).

Table 1
Comparisons of characteristics between patients with APAC included from the post-restriction and control periods.

Parameter	Patients with APAC included from the post-restriction period (N = 189)	Patients with APAC included from the control period (N = 51)	*P*-value
Age (IR), years	67.6 (62.8, 72.0)	69.0 (64.2, 76.0)	0.043[a]
Sex			
Male (%)	38 (20.1)	11 (21.6)	0.818[b]
Female (%)	151 (79.9)	40 (78.4)	
Eyes with APAC attack			
One eye (%)	159 (84.1)	48 (94.1)	0.066[c]
Both eyes (%)	30 (15.9)	3 (5.9)	
Ratio of APAC in glaucoma department (%)	189/321 (58.9)	51/331 (15.4)	< 0.001[b]
TST (IR), hours	120.0 (24.0, 240.0)	48.0 (24.0, 168.0)	0.039[a]
Hypertension			
No (%)	115 (60.8)	29 (56.9)	0.606[b]
Yes (%)	74 (39.2)	22 (43.1)	
Diabetes			
No (%)	165 (87.3)	48 (94.1)	0.172[c]
Yes (%)	24 (12.7)	3 (5.9)	

APAC, acute primary angle closure; IR, interquartile range; TST, time from symptom onset to treatment.
[a] Mann–Whitney *U* test.
[b] χ^2 test.
[c] Fisher's exact test.

Table 2
Comparisons of vision and IOP assessed at diagnosis and after initial interventions between APAC eyes included during the post-restriction and control periods.

Condition	Parameter	APAC eyes included from the post-restriction period (N = 219)	APAC eyes included from the control period (N = 54)	*P*-value
At diagnosis	PVA (IR), LogMar	1.10 (0.70, 2.70)	1.26 (0.60, 2.40)	0.796[a]
	Rate of blindness (PVA ≤ Snellen 3/60) (%)	102 (46.6)	25 (46.3)	0.971[b]
	IOP (IR), mmHg	41.1 (30.5, 48.0)	41.0 (32.8, 48.0)	0.974[a]
After initial interventions	PVA (IR), LogMar	0.70 (0.40, 1.30)	0.56 (0.30, 1.00)	0.297[a]
	Rate of blindness (PVA ≤ Snellen 3/60) (%)	50 (22.8)	10 (18.5)	0.436[b]
	BCVA (IR), LogMar	0.40 (0.22, 1.30)	0.40 (0.21, 1.00)	0.504[a]
	Rate of blindness (BCVA ≤ Snellen 3/60) (%)	43 (19.6)	10 (18.5)	0.784[b]
	SE (IR), diopter	1.38 (0.63, 2.38)	1.25 (0.13, 2.75)	0.605[a]
	IOP (IR), mmHg	15.1 (13.0, 29.0)	14.0 (12.0, 25.4)	0.293[a]

IOP, intraocular pressure; APAC, acute primary angle closure; PVA, presenting visual acuity; IR, interquartile range; LogMar, logarithm of the minimum angle of resolution; BCVA, best-corrected visual acuity; SE, spherical equivalent.
[a] Mann–Whitney test.
[b] χ^2 test.

3.3. Factors associated with APAC during the post-restriction period

According to the univariate and multivariate logistic regression analyses, the predictors associated with the occurrence of APAC during the COVID-19 post-restriction period were shorter AL (OR, 0.423; 95 % CI, 0.217–0.825; $P = 0.012$), larger PD (OR, 1.442; 95 % CI, 1.037–2.004; $P = 0.029$), and poorer MD (OR, 0.936; 95 % CI, 0.882–0.993; $P = 0.028$) (Table 4).

3.4. Initial interventions for APAC eyes during the two periods

Table 5 summarizes the numbers and proportions of APAC eyes receiving different initial interventions during the two periods. There were no significant differences in the choices of initial interventions among APAC eyes during the two periods ($P = 0.489$). The ratios of IOP control (IOP <21 mmHg) were not significantly different among the different choices of initial interventions ($P = 0.815$).

3.5. Questionnaire responses from APAC patients during the post-restriction period

Of the 189 patients with APAC included during the post-restriction period, 151 patients completed the questionnaires. Among them, 130 patients with APAC were diagnosed with concurrent COVID-19 infection (88 patients presented with APAC concurrently with COVID-19 infection and 42 afterward), of which 54 (41.5 %) had coughing and/or vomiting as the main symptoms. Of these, 89.2 % spent 0 h per day on outdoor activity; 44.6 % drank more water than usual, with 14.6 % drinking more than twice the amount of water than usual; 91.5 % used antipyretics; and 20.0 % had mood swings, including anxiety, depression, and tension, during the concurrent COVID-19 infection.

Table 3
Comparisons of ocular parameters assessed after initial interventions between APAC eyes included during the post-restriction and control periods.

Parameter	APAC eyes included from the post-restriction period (N = 219)	APAC eyes included from the control period (N = 54)	*P*-value
Corneal endothelial cell count (IR),/mm (Liang et al.2021)	2293.6 (1614.8, 2648.1)	2444.2 (1933.5, 2718.1)	0.117[a]
AK (IR), diopter	44.41 (43.46, 45.90)	44.32 (43.06, 45.47)	0.342[a]
CCT (IR), μm	570.5 (535.0, 609.8)	557.5 (535.3, 598.0)	0.400[a]
Central ACD (IR), mm	2.13 (1.96, 2.29)	2.16 (1.94, 2.38)	0.485[a]
LT (IR), mm	5.09 (4.82, 5.38)	5.16 (4.81, 5.56)	0.731[a]
AL (IR), mm	22.24 (21.64, 22.74)	22.57 (22.11, 23.20)	0.002[a]
PD (IR), mm	5.20 (4.25, 6.20)	4.40 (3.10, 5.50)	0.004[a]
VCDR (IR)	0.40 (0.30, 0.60)	0.30 (0.30, 0.50)	0.004[a]
Ratio of GON (%)	85/171 (49.7)	12/39 (30.8)	0.032[b]
MD (IR), dB	−18.07 (−26.66, −7.93)	−10.16 (−18.52, −3.69)	0.003[a]
VFI (IR), %	57.0 (19.0, 88.0)	83.5 (53.5, 96.0)	0.007[a]

APAC, acute primary angle closure; IR, interquartile range; AK, average keratometry; CCT, central corneal thickness; ACD, anterior chamber depth; LT, lens thickness; AL, axial length; PD, pupil diameter; VCDR, vertical cup disc ratio; GON, glaucomatous optic neuropathy; MD, mean deviation; VFI, visual field index.
[a] Mann–Whitney *U* test.
[b] χ^2 test.

Table 4
Results of the univariate and multivariate logistic regression analyses of the occurrence of APAC during the COVID-19 post-restriction period.

Variable	Univariate logistic regression		Multivariate logistic regression			
	OR (95 % CI)	*P*-value	Estimated regression coefficient	OR (95 % CI)	*P*-value	VIF
Corneal endothelial cell count,/mm	1.000 (0.999, 1.000)	0.089				
AK, diopter	1.123 (0.919, 1.371)	0.257				
CCT, μm	1.001 (0.996, 1.005)	0.780				
Central ACD, mm	0.640 (0.252, 1.623)	0.347				
LT, mm	1.003 (0.606, 1.661)	0.991				
AL, mm	0.531 (0.356, 0.791)	0.002	−0.860	0.423 (0.217, 0.825)	0.012	1.041
PD, mm	1.376 (1.102, 1.719)	0.005	0.366	1.442 (1.037, 2.004)	0.029	1.028
VCDR	10.453 (1.903, 57.437)	0.007	–	–	–	1.043
GON, present	2.224 (1.058, 4.676)	0.035	–	–	–	1.057
MD, dB	0.932 (0.886, 0.980)	0.006	−0.066	0.936 (0.882, 0.993)	0.028	1.094
VFI, %	0.982 (0.967, 0.996)	0.013	–	–	–	–

APAC, acute primary angle closure; COVID-19, coronavirus disease 2019; AK, average keratometry; CCT, central corneal thickness; ACD, anterior chamber depth; LT, lens thickness; AL, axial length; PD, pupil diameter; VCDR, vertical cup disc ratio; GON, glaucomatous optic neuropathy; MD, mean deviation; VFI, visual field index.
The VFI values were not included in the multivariate logistic regression because of the collinearity with the MD values.

Table 5
Initial interventions for APAC eyes included during the post-restriction and control periods.

Initial interventions	APAC eyes included from the post-restriction period (N = 219)	APAC eyes included from the control period (N = 54)	*P*-value 1	Ratio of IOP control (%) in all included APAC eyes (IOP <21 mmHg)	*P*-value 2
Medications (%)	137 (62.6)	31 (57.4)	0.489	60/168 (35.7)	0.815
Medications + laser (%)	52 (23.7)	17 (31.5)		22/69 (31.9)	
Medications + surgery (+laser) (%)	30 (13.7)	6 (11.1)		13/36 (36.1)	

APAC, acute primary angle closure; IOP, intraocular pressure.
Laser = laser peripheral iridotomy and/or argon laser peripheral iridoplasty; surgery = anterior chamber paracentesis or peripheral iridectomy.
P-value 1: *P*-value of the χ^2 test for comparison of different initial interventions between APAC eyes included from the post-restriction and control periods.
P-value 2: *P*-value of the χ^2 test for comparison of ratios of IOP control between four different initial interventions.

4. Discussion

In this multi-center study, we observed an increase in the overall and individual numbers of patients with APAC at the two hospitals identified during the post-restriction period compared to the control period in Northern China. Furthermore, the ratios of patients with APAC among the overall patients at the glaucoma departments of the two hospitals also increased during the post-restriction period, compared with those during the control period, with similar numbers of total glaucoma department visitors between the two periods. Similarly, Ying et al. noted a higher incidence of APAC triggered or aggravated by COVID-19 infection. However, our study is the first to comprehensively characterize the clinical features of these patients and identify potential risk factors using a large sample across two eye centers.

Patients with APAC during the post-restriction period were found to be younger, with no significant differences in sex prevalence and presence of systemic diseases, including hypertension and diabetes, compared with the control period. Additionally, there was a tendency for an increased number of patients to have bilateral eye involvement during the post-restriction period, with no significant difference from that during the control period. Older age is the main risk factor for APAC attacks; however, in our study, an increased number of younger patients with APAC indicated that other ocular anatomic characteristics and risk factors, such as choroidal engorgement and expansion or psychological and physiologic changes affecting the whole body, may play an important role in the development of APAC, considering the tendency of increased cases of bilateral involvement [30–33].

Our study found a longer TST in patients with APAC during the post-restriction period than in those during the control period (120 h vs. 48 h), which might have been caused by reduced healthcare resources and increased traffic due to the COVID-19 pandemic, as well as reluctance to visit the emergency department for fear of COVID-19 infection. However, there were no significant differences in visual acuity, IOP, and rates of blindness at diagnosis and after initial interventions between patients with APAC during the two periods.

No significant difference was found in CCT, AK, central ACD, and LT between patients with APAC during the two periods in our study. However, APAC eyes identified during the post-restriction period showed a shorter AL, larger PD, larger VCDR, and worse MD and VFI values in visual field testing than those identified during the control period. Moreover, shorter AL, larger PD and worse MD were determined to be potential factors associated with the occurrence of APAC during the COVID-19 post-restriction period using logistic regression analysis. These findings revealed that more patients with APAC during the post-restriction period had experienced a chronic IOP-increasing process or had one or several smaller acute attacks before the post-restriction period, which may also partly explain the paradox of a longer TST but no poorer visual acuity or higher rate of blindness in patients with APAC during the post-restriction group. These findings highlight the need for close monitoring and aggressive management of APAC cases during the pandemic to prevent irreversible optic nerve damage. Previous chronic IOP rises or smaller acute attacks make the eye less vulnerable to high IOP or a longer TST [34]. Moreover, a larger PD may be related to a longer TST with a longer high-IOP persistent time. Ying et al. found that COVID-19 positive APAC eyes exhibited larger PD and deeper ACD compared to COVID-19 negative eyes, suggesting the infection could potentially alter anterior segment anatomy [6]. Hence, future studies evaluating how COVID-19 may modify anterior segment structures and ocular surface homeostasis could provide novel mechanistic insights into the ocular effects of this virus and their possible contributions to APAC risk.

Although the initial APAC treatments in our study lacked consensus, the principal aim remained rapid initial reduction of IOP, thereby preventing further optic nerve damage [35]. Hence, although some differences existed in the manifestations in patients APAC during the two periods, there were no significant differences in the choices of initial interventions among APAC eyes during the two periods. Definitive treatment, such as laser peripheral iridotomy and lens extraction, followed once the corneal edema was reduced using topical and systematic IOP-lowering medication. Among the 273 APAC eyes included, 61.5 % were treated only with IOP-reducing medications and 34.8 % were treated with IOP-reducing medications plus laser (laser peripheral iridotomy and/or argon laser peripheral iridoplasty) or surgery (anterior chamber paracentesis or peripheral iridectomy). Only 3.7 % were treated with a combination of IOP-reducing medications, laser, and surgery. There was no significant difference in the IOP control rates among the different initial interventions.

Based on findings from the questionnaire survey, some symptoms and behavioral and psychological changes concurrent with COVID-19 infection might have contributed to an APAC attack. For example, 41.5 % of patients with APAC had coughing and/or vomiting as one of the main symptoms. These Valsalva maneuvers caused by vigorous coughing or vomiting might cause significant elevation of the IOP, narrowing of the anterior chamber angle recess, thickening of the ciliary body, and increased iris thickness, contributing to an APAC attack [18]. Furthermore, 89.2 % of patients with APAC reported spending 0 h per day on outdoor activities during the post-restriction period. APAC tends to occur more commonly during winter, which may be related to prolonged indoor time with poor light acting as a darkroom provocative test [18,36,37]. Moreover, 44.6 % of patients with APAC reported drinking more water than usual, with 14.6 % drinking approximately twice or more than usual, which may cause increased choroidal thickness and contribute to angle closure and IOP increase [38,39].

Many studies have shown that the COVID-19 pandemic leads to psychological distress, which could also be a predisposing factor for APAC [2]. In our study, 20 % of patients with APAC reported mood swings, including anxiety, depression, and tension, during the post-restriction period. Emotional processes can influence pupillary changes and choroidal thickness through the autonomic nervous system, causing pupillary block and choroidal engorgement and expansion, leading to an APAC attack [18].

Of the included patients with APAC during the post-restriction period, 91.5 % reported using antipyretics during COVID-19 infection. Several case reports showed that some drugs used during the COVID-19 pandemic, such as antitussive and nasal decongestants, promethazine compound linctus, diphenhydramine compound linctus, acetified syrup (containing pseudoephedrine and triprolidine), chlorpheniramine, different types of anti-histamines, and even COVID-19 vaccination, may cause secondary APAC [11,40,41]. We could not find a definite relationship between certain drug use in our study and increased cases of APAC since the recall of medications used by patients may not have been accurate.

The strength of our study was that it was a multi-center study that included comprehensive data from two hospitals during the same period from different years under different COVID-19-related policies to investigate the increased number and related characteristics of patients with APAC during the post-restriction period.

Our study also had some limitations. First, according to telephone surveys, 8 and 10 patients with APAC were transferred to HCEH and QEH, respectively, because of temporary shut-down or strained medical resources in other hospitals during the post-restriction period, which may have influenced the results. Second, comparing ocular biometric parameters in eyes that underwent different initial interventions might cause bias and future studies aim to evaluate these parameters in a more homogeneous population, ideally prior to any intervention, to minimize potential confounding. Third, we could not provide the information referring to the proportion of the patients with confirmed/suspected infection or whether APAC accompanied COVID-19 infection in included patients since not all the patients received the COVID-19 antigen or nucleic acid tests in our study. And the information referring to COVID-19 infection obtained from self-reported questionnaires might also cause a bias. Fourth, we could not assess the exact influence of all risk factors on APAC occurrence during the post-restriction period, but only the possible relationships. Fifth, Fig. 1, which demonstrated the relationship between COVID-19 cases and patients with APAC during the post-restriction and control periods, relied on nationwide COVID-19 case data instead of city-specific case data. Future studies should strive to obtain more localized COVID-19 data when available to strengthen the analysis of potential associations between COVID-19 prevalence and APAC incidence. Last, data collected from the two eye centers in our study may not fully capture the presenting trends of APAC across all regions of China. Future studies incorporating data from other regions of China would provide an even more robust evaluation of the associations between COVID-19 outbreaks and APAC presentation.

In conclusion, during the COVID-19 post-restriction period, APAC cases were increased compared with those during the control period. Patients with APAC during the post-restriction period were younger and had a longer TST, a higher prevalence of GON, larger PD, shorter AL, and worse visual field test results. Behavioral and psychological changes concurrent with COVID-19 infection under these special circumstances might act as predisposing factors for an APAC attack. Before major disease outbreaks, targeting the population at high risk of certain diseases should be considered.

Funding

None.

Ethics approval

The ethics committees of HCEH (approval ID: 2023002) and QEH (approval ID: 202,329) approved the study. This study adhered to the principles of the Declaration of Helsinki. The requirement for informed consent was waived due to the retrospective nature of the study.

Data sharing statement

The authors declare that all data supporting he findings of this study are available within the paper. They are not publicly available, and restrictions apply to their use. All requests would require evaluation on an individual basis and can be made by contacting wningli@vip.163.com.

CRediT authorship contribution statement

Ye Zhang: Writing – original draft, Methodology, Investigation, Formal analysis, Conceptualization. **Su Jie Fan:** Resources, Project administration, Investigation. **Xiao Jing Pan:** Resources, Project administration, Investigation. **Zhi Hong Zhang:** Project administration, Investigation. **Qing Shu Ge:** Project administration, Investigation. **Jin Wang:** Investigation. **Yue Wang:** Investigation. **Ming Guang He:** Writing – review & editing, Investigation. **Ning Li Wang:** Writing – review & editing, Validation, Supervision, Resources, Investigation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e34090.

References

[1] K. Cao, B. Kline, Y. Han, G.S. Ying, N.L. Wang, Current evidence of 2019 Novel Coronavirus Disease (COVID-19) ocular transmission: a systematic review and meta-analysis, BioMed Res. Int. 2020 (2020) 7605453.
[2] V. Violant-Holz, M.G. Gallego-Jiménez, C.S. González-González, S. Muñoz-Violant, M.J. Rodríguez, O. Sansano-Nadal, et al., Psychological health and physical activity levels during the COVID-19 pandemic: a systematic review, Int. J. Environ. Res. Publ. Health 17 (2020) 9419.
[3] V. Haldane, C. De Foo, S.M. Abdalla, A.-S. Jung, M. Tan, S. Wu, et al., Health systems resilience in managing the COVID-19 pandemic: lessons from 28 countries, Nat. Med. 27 (2021) 964–980.
[4] W.N. Liang, J.H. Yao, J. Wu, X. Liu, J. Liu, L. Zhou, et al., Experience and thinking on the normalization stage of prevention and control of COVID-19 in China, Zhonghua Yixue Zazhi 101 (2021) 695–699.
[5] J. Liu, M. Liu, W. Liang, The dynamic COVID-zero strategy in China, China CDC Wkly 4 (2022) 74–75.
[6] Chinese Government, Notice on further optimizing the implementation of COVID-19 prevention and control measures, Provincial Henan Government. People's Government. Henan Has Passed the Epidemic Peak (2022). http://www.gov.cn/xinwen/2022-12/07/content_5730443.htm. https://www.henan.gov.cn/2023/01-09/2669240.html, 2023 [accessed 14 January 2023].
[7] S. Huang, Z. Gao, S. Wang, China's COVID-19 reopening measures-warriors and weapons, Lancet 401 (2023) 643–644.
[8] World Health Organization. Coronavirus Disease (COVID-19) Situation Dashboard, https://covid19. http://who.int/.
[9] Y. Ying, R. Zhai, Y. Sun, Q. Sheng, X. Fan, X. Kong, The occurrence of acute primary angle closure triggered, aggravated, and accelerated by COVID-19 infection: retrospective observational study, Front. Public Health 11 (2023) 1196202.
[10] M. Zhu, Y. Yan, The surge of acute angle-closure glaucoma during the outbreak of Omicron in a tertiary hospital in Shanghai, Graefes Arch. Clin. Exp. Ophthalmol. 261 (2023) 2709–2711.
[11] S.C.L. Au, From acute angle-closure to COVID-19 during Omicron outbreak, Vis J Emerg Med 29 (2022) 101514.
[12] G. Barosco, R. Morbio, F. Chemello, R. Tosi, G. Marchini, Bilateral angle-closure during hospitalization for coronavirus disease-19 (COVID-19): a case report, Eur. J. Ophthalmol. 32 (2022) NP75–82.
[13] S.H. Chen, R. Karanjia, R.L. Chevrier, D.H. Marshall, Bilateral acute angle closure glaucoma associated with hydrochlorothiazide-induced hyponatraemia, BMJ Case Rep. 2014 (2014) bcr2014206690.
[14] B.D. Krawitz, P. Sirinek, D. Doobin, T. Nanda, M. Ghiassi, J.D. Horowitz, et al., The challenge of managing bilateral acute angle-closure glaucoma in the presence of active SARS-CoV-2 infection, J. Glaucoma 30 (2021) e50–e53.
[15] R.R. Nerlikar, A.C. Palsule, S. Vadke, Bilateral acute angle closure glaucoma after prone position ventilation for COVID-19 pneumonia, J. Glaucoma 30 (2021) e364–e366.
[16] S. Özmen, N.O. Aksoy, B. Çakır, G. Alagöz, Acute angle-closure glaucoma concurrent with COVID 19 infection; case report, Eur. J. Ophthalmol. 33 (2023) NP42–45.
[17] S.J. Gedde, P.P. Chen, K.W. Muir, K. Vinod, J.T. Lind, M.M. Wright, et al., Primary angle-closure disease preferred practice pattern, Ophthalmology 128 (2021) P30–P70.

[18] X. Zhang, Y. Liu, W. Wang, S. Chen, F. Li, W. Huang, et al., Why does acute primary angle closure happen? Potential risk factors for acute primary angle closure, Surv. Ophthalmol. 62 (2017) 635–647.

[19] E.W. Chan, X. Li, Y.C. Tham, J. Liao, T.Y. Wong, T. Aung, et al., Glaucoma in Asia: regional prevalence variations and future projections, Br. J. Ophthalmol. 100 (2016) 78–85.

[20] Y. Lachkar, W. Bouassida, Drug-induced acute angle closure glaucoma, Curr. Opin. Ophthalmol. 18 (2007) 129–133.

[21] B.G. Shily, Psychophysiological stress, elevated intraocular pressure, and acute closed-angle glaucoma, Optom. Vis. Sci. 64 (1987) 866–870.

[22] R. Sihota, T. Dada, A. Aggarwal, G. Srinivasan, V. Gupta, V.K. Chabra, Does an iridotomy provide protection against narrowing of the anterior chamber angle during Valsalva maneuvre in eyes with primary angle closure, Eye 22 (2008) 389–393.

[23] S.C.L. Au, Cluster of ocular acute primary angle closure cases and increased antitussive or nasal decongestants usage following the surge in acute COVID-19 infection, QJM 116 (2023) 601–602.

[24] L.P. Ang, T. Aung, P.T. Chew, Acute primary angle closure in an Asian population: long-term outcome of the fellow eye after prophylactic laser peripheral iridotomy, Ophthalmology 107 (2000) 2092–2096.

[25] A. Akman, L. Asena, S.G. Güngör, Evaluation and comparison of the new swept source OCT-based IOLMaster 700 with the IOLMaster 500, Br. J. Ophthalmol. 100 (2016) 1201–1205.

[26] J. Huang, Y. Zhao, G. Savini, G. Yu, J. Yu, Z. Chen, et al., Reliability of a new swept-source optical coherence tomography biometer in healthy children, adults, and cataract patients, J Ophthalmol 2020 (2020) 8946364.

[27] H. Ho, P.T. Chew, C. Sng, H. Huang, T. Aung, S.A. Perera, A comparison of two approaches to managing acute primary angle closure in Asian eyes, Clin. Ophthalmol. 7 (2013) 1205–1210.

[28] Y. Zhang, Q. Zhang, S.Z. Li, M.G. He, S.N. Li, N.L. Wang, Anterior segment characteristics and risk factors for primary angle closure disease with long axial lengths: the Handan Eye Study, Invest. Ophthalmol. Vis. Sci. 64 (2023) 8.

[29] D. Pascolini, S.P. Mariotti, Global estimates of visual impairment: 2010, Br. J. Ophthalmol. 96 (2012) 614–618.

[30] M. Baskaran, R.C. Foo, C.Y. Cheng, A.K. Narayanaswamy, Y.-F. Zheng, R. Wu, et al., The prevalence and types of glaucoma in an urban Chinese population: the Singapore Chinese eye study: the Singapore Chinese eye study, JAMA Ophthalmol 133 (2015) 874–880.

[31] P.J. Foster, F.T. Oen, D. Machin, T.P. Ng, J.G. Devereux, G.J. Johnson, et al., The prevalence of glaucoma in Chinese residents of Singapore: a cross-sectional population survey of the Tanjong Pagar district, Arch. Ophthalmol. 118 (2000) 1105–1111.

[32] Y.C. Ko, C.J. Liu, W.M. Hsu, C.Y. Cheng, T.M. Kuang, P. Chou, Determinants and characteristics of angle-closure disease in an elderly Chinese population, Ophthalmic Epidemiol. 22 (2015) 109–115.

[33] W. Wang, M. Zhou, W. Huang, S. Chen, X. Ding, X. Zhang, Does acute primary angle-closure cause an increased choroidal thickness? Invest. Ophthalmol. Vis. Sci. 54 (2013) 3538–3545.

[34] A. Li, X. Zhang, D. Zheng, J. Ge, A.M. Laties, C.H. Mitchell, Sustained elevation of extracellular ATP in aqueous humor from humans with primary chronic angle-closure glaucoma, Exp. Eye Res. 93 (2011) 528–533.

[35] P.P. Chan, J.C. Pang, C.C. Tham, Acute primary angle closure-treatment strategies, evidences and economical considerations, Eye 33 (2019) 110–119.

[36] J.S. Hillman, J.D. Turner, Association between acute glaucoma and the weather and sunspot activity, Br. J. Ophthalmol. 61 (1977) 512–516.

[37] R. Aparna, G. Lisika, Acute angle closure epidemic during COVID-19 pandemic, EyeQuest 47 (2022) 39–44.

[38] C.G.V. De Moraes, A.S.C. Reis, A.F. de Sá Cavalcante, M.E. Sano, R. Susanna Jr., Choroidal expansion during the water drinking test, Arbeitsphysiologie 247 (2009) 385–389.

[39] H.A. Quigley, D.S. Friedman, N.G. Congdon, Possible mechanisms of primary angle-closure and malignant glaucoma, J. Glaucoma 12 (2003) 167–180.

[40] J.S.M. Lai, R.A. Gangwani, Medication-induced acute angle closure attack, Hong Kong Med. J. 18 (2012) 139–145.

[41] Y. Salem Mahjoubi, I. Dahmani, I. Souilem, et al., Acute angle closure glaucoma following COVID-19 vaccination, Therapie 7 (23) (2023) S0040–S5957, 00082-3.