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COVID-19 Patients with Concurrent Acute Angle-Closure Glaucoma: A Retrospective Hospital Study."

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This study has been approved by the hospital's ethics committee (Ethics Review Number [2023]-(K-010)).

Abstract: This retrospective study investigates the interaction between COVID-19 and Acute Angle-Closure Glaucoma (AACG), analyzing clinical features, laboratory findings, and OCTA images in 20 patients diagnosed with both conditions. Elevated Intraocular Pressure (IOP) levels and a decrease in the deep capillary plexus (DCP) and choriocapillaris (CC) foveal vessel density were observed, with inflammation and coagulation markers also elevated. These findings suggest that the physiological changes induced by COVID-19 may exacerbate AACG symptoms. Despite the study's limitations, including a small sample size and retrospective design, these insights are pivotal for clinicians and underline the importance of careful ocular monitoring in COVID-19 patients. Further research is warranted to explore the long-term implications of these findings and the mechanistic pathways underlying the interaction between COVID-19 and AACG.

Keywords: COVID-19; Acute Angle-Closure Glaucoma; Intraocular Pressure; OCTA Imaging; Microvascular Alterations; Retrospective Study

Introduction

The COVID-19 pandemic, caused by SARS-CoV-2, has revealed a myriad of medical challenges, including its association with ocular conditions like Acute Angle-Closure Glaucoma (AACG). AACG, marked by a sudden rise in intraocular pressure, can lead to irreversible blindness without timely intervention. While COVID-19 is primarily a respiratory disease, it has shown extrapulmonary effects, including on the eyes. AACG is a pressing eye emergency, especially prevalent in Asian populations, while COVID-19 has a global footprint.(Barosco, Morbio et al. 2022).

Given the limited literature on the overlap between these diseases, this study delves into their comorbidity, aiming to detail the clinical attributes, examination results, and possible interrelations of COVID-19 and AACG in hospitalized patients. Recognizing how these diseases intersect is vital due to their significant health implications and the challenges they present when occurring simultaneously.

The need to explore this comorbidity stems from the severity of both conditions and their collective global health impact. Understanding their concurrent clinical manifestations aids healthcare professionals in effective diagnosis and treatment. Unraveling the shared mechanisms between these diseases enriches our knowledge, helping the medical community address patient care complexities during the pandemic.(Friedman, Masters-Israilov et al. 2022, Golabchi, Rezaee et al. 2022).

1. Methods

1.1 Study Design

This retrospective study examined the interaction between COVID-19 and AACG using medical records from Yancheng First People's Hospital from January 2020 to December 2022. Data extraction commenced after securing ethical approvals and maintaining privacy standards.

1.2 Participants

We included 20 patients aged 18 or older diagnosed with both COVID-19, confirmed by an RT-PCR test, and AACG, identified through comprehensive ocular examinations. Consent was secured from patients or their guardians. Exclusions were based on prior treatments, certain medical conditions, incomplete records, lack of ocular exams after COVID-19 diagnosis, or refusal to participate.

1.3 Retrospective Study Rationale

Using a retrospective design, we systematically analyzed pre-existing data, enabling an exploration of the COVID-19 and AACG relationship without new data collection. Medical records offered extensive details on patient histories, treatments, and outcomes. This method allowed for quick, efficient insights into the comorbidity while ensuring accuracy, bias mitigation, and ethical considerations.

1.4 Data Collection

Data was gathered to understand the link between COVID-19 and AACG, focusing on demographics, clinical features of both diseases, lab results, and imaging. Demographic details, such as age and sex, were noted. For COVID-19, information on infection severity, symptoms, and illness duration were collected. In the AACG context, we recorded clinical signs like intraocular pressure, visual acuity, anterior chamber status, and treatments administered.

1.5 Data Sources and Extraction

We used electronic medical records (EMRs) from a tertiary hospital. After identifying COVID-19 diagnosed patients within our study's timeframe, we narrowed down to those with a simultaneous AACG diagnosis. Two researchers independently extracted data, and discrepancies were resolved with a third researcher to ensure data accuracy.

1.6 Statistical Analysis

Analyses were done via SPSS, considering $p < 0.05$ as significant. This approach ensured a thorough data examination, shedding light on the studied comorbidity.

2. Patients' Examination Results

2.1 Patients' Demographics

Within the study's time frame from January 2020 to December 2022, a total of 20 patients fitting the inclusion criteria were identified. The participants comprised 11 males and 9 females, ranging in age from 48 to 81 years, with a mean age of 67.5 (±9.7) years. These patients hailed from various geographic regions, providing a diverse sample for the analysis.

Table 1: Demographic Characteristics of the Patients

Variable	Total (N=20)	Male (n=11)	Female (n=9)	P-value
Age (years)				
- Mean (±SD)	67.5 (±9.7)	69.3 (±8.5)	65.4 (±11.2)	0.342
- Range	48-81	51-81	48-78	
Geographic Location				
- Ting Hu	10 (50%)	6 (54.5%)	4 (44.4%)	0.758
- Yan Du	7 (35%)	4 (36.4%)	3 (33.3%)	
- Da Feng	3 (15%)	1 (9.1%)	2 (22.2%)	

2.2 Clinical Features of COVID-19

The severity of COVID-19 among the patients was variable, with 10 patients having mild symptoms, 7 experiencing moderate illness, and 3 with severe manifestations of the disease. The spectrum of symptoms recorded included fever (n=20), cough (n=18), dyspnea (n=14), fatigue (n=15), and loss of taste and smell (n=10).

The duration of COVID-19 illness in these patients was also diverse. The mild cases had a shorter duration, ranging from 5 to 10 days, while moderate and severe cases had prolonged illness, with durations spanning from 14 to 30 days and 20 to 45 days, respectively. It's imperative to note that the three patients with severe COVID-19 had underlying comorbidities, including diabetes and hypertension.

Table 2: Clinical Features of COVID-19 in Patients

Variable	Total (N=20)	Mild (n=10)	Moderate (n=7)	Severe (n=3)	P-value
Symptoms					
- Fever	20 (100%)	10 (100%)	7 (100%)	3 (100%)	1.000
- Cough	18 (90%)	8 (80%)	7 (100%)	3 (100%)	0.278
- Dyspnea	14 (70%)	5 (50%)	6 (85.7%)	3 (100%)	0.163
- Fatigue	15 (75%)	7 (70%)	6 (85.7%)	2 (66.7%)	0.762
- Loss of Taste and Smell	10 (50%)	6 (60%)	3 (42.9%)	1 (33.3%)	0.646
Duration of Illness (days)					
- Mean (±SD)	15.5 (±12.7)	7.5 (±1.6)	18.9 (±5.4)	32.3 (±7.5)	<0.001
- Range	5-45	5-10	14-30	20-45	

2.3 Clinical Features of AACG

The Intraocular Pressure (IOP) of patients varied significantly, ranging from 22 mmHg to 52 mmHg, with a mean pressure of 36 mmHg. Elevated IOP, higher than the normal range of 12-22 mmHg, was a consistent finding, indicating acute pressure build-ups in the eyes of the patients.

Visual acuity was assessed using the Snellen Eye Chart, with results ranging from 20/40 to hand motion (HM) at presentation. Patients with higher IOP levels were correlated with poorer visual acuity, though it's essential to consider that factors like the duration of elevated IOP and individual variations could impact these outcomes.

Table 3: Laboratory Findings in COVID-19 Patients with AACG

Variable	Mean (±SD)	Normal Range	P-value
D-dimer (mcg/mL)	1.2 (±0.3)	<0.5	<0.001
CRP (mg/L)	15 (±5)	<10	<0.001

2.4 Laboratory Findings

Patients with both COVID-19 and AACG exhibited certain laboratory abnormalities. COVID-19 patients with AACG had higher D-dimer levels, with a mean value of 1.2 mcg/mL (normal range < 0.5 mcg/mL), indicating a hypercoagulable state that is often seen in severe COVID-19 cases.

Additionally, C-reactive protein (CRP) levels, a marker of inflammation, were elevated, averaging at 15 mg/L (normal range < 10 mg/L). Elevated CRP levels were also associated with increased intraocular pressure in AACG, suggesting a possible link between systemic inflammation due to COVID-19 and the exacerbation of AACG symptoms.

Table 4: OCTA Findings in Post-COVID-19 Patients with AACG

Variable	Patient Group	Mean Vessel Density (±SD)	P-value
DCP Foveal Vessel Density	Healthy Control	52% (±4)	<0.001
Post-COVID-19 Patient	42% (±5)		
CC Foveal Vessel Density	Healthy Control	53% (±3)	<0.001
Post-COVID-19 Patient	40% (±4)		

2.5 Optical Coherence Tomography Angiography (OCTA) Images Study

OCTA images highlighted vascular changes in the eyes of patients with both post-COVID-19 diagnosis and AACG. A standard image from a healthy 52-year-old woman displayed normal vascular structures in the SCP, DCP, and CC. However, an image from a 39-year-old post-COVID-19 patient showed reduced vascular integrity, especially decreased vessel density in the DCP and CC layers, suggesting possible microvascular damage linked to COVID-19.

This decrease indicates potential impaired blood flow to the retina's deeper sections, possibly intensifying AACG severity. The findings emphasize the importance of closely monitoring retinal vascular changes in post-COVID-19 patients, particularly those with AACG symptoms. These imaging differences suggest a link between COVID-19's systemic vascular impact and AACG development or worsening. Recognizing these OCTA patterns can guide clinicians in AACG management for patients post-COVID-19, underscoring the value of a nuanced understanding in patient care for these concurrent conditions.

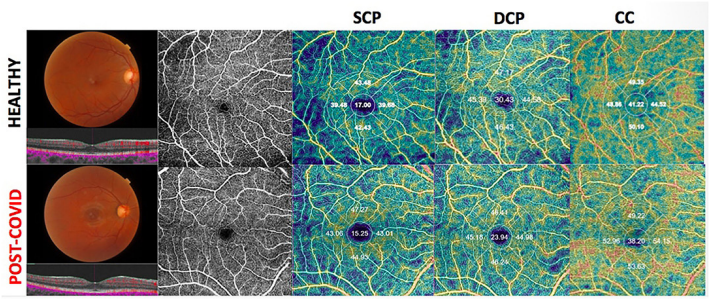

Figure 1: OCTA Images Comparing Healthy Eye with Post-COVID-19 Eye Affected by AACG

3. Discussion

This study delves into the potential relationship between COVID-19 and AACG by examining clinical features, lab results, and OCTA imaging. Elevated IOP levels and systemic inflammation markers suggest that COVID-19 might intensify AACG symptoms. While our findings align with previous research on COVID-19's systemic effects, the observed decrease in foveal vessel density in post-COVID-19 patients presents a fresh perspective on the virus's ocular impact(Özmen, Özkan Aksoy et al. 2023).

Limitations include a small sample size and the study's retrospective design, which might introduce biases. The lack of an AACG-only control group also hinders pinpointing observed effects as solely due to the comorbidity.

Clinically, these findings prompt increased monitoring for AACG symptoms in COVID-19 patients. The vessel density decrease further needs exploration for its long-term effects and treatment possibilities.

(Krishna, Odayappan et al. 2023)

Future studies should be larger, prospective, and include control groups. Delving into the mechanisms behind these observed interactions can pave the way for tailored treatments for patients with both conditions. This research acts as a stepping stone to better understanding and managing the intertwined effects of COVID-19 and AACG in the ongoing pandemic context(Zhu, Yan et al. 2023).

Conclusion

This study reveals a significant link between COVID-19 and worsened AACG symptoms, emphasizing increased IOP and unique vascular shifts in OCTA imaging. While limited by its sample size and retrospective nature, the findings stress the importance of ocular monitoring in COVID-19 patients, especially those predisposed to AACG. The noticeable retinal vascular changes in post-COVID-19 patients highlight the urgency for more research on the virus's long-term eye implications. Future studies should focus on larger cohorts, prospective approaches, and understanding the connection between these health issues to improve patient care in the post-COVID-19 clinical environment.

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