Ocular Symptoms Assessment of COVID-19: A Cross-Sectional Study

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Abstract

Objective: To assess the clinical manifestations of coronavirus disease-19 (COVID-19) infection and the characteristics of ocular involvement.

Methods: In this cross-sectional descriptive study, an online questionnaire was performed on reverse transcriptase-polymerase chain reaction (RT-PCR) positive confirmed COVID-19 patients who do not require supplemental oxygen therapy and are registered to the home isolation program or admitted to Thammasat University Hospital in Thailand from September to November 2022. The baseline ocular and systemic history was compared to that of the COVID-19 period, and vaccination history was collected. Binary and categorical response data were shown as a percentage and proportions. Quantitative data were presented as means and standard deviations. McNemar test was used to assess the COVID ocular symptoms during the infectious period. Odds Ratio with 95% confidence interval was calculated to study the relationship between ocular severity symptoms and vaccination. *P*-value < .05 was considered statistically significant.

Results: A total of 189 COVID-19 patients (32.3% male and 67.7% female) were enrolled in the study and completed an online questionnaire. The mean age of the patients was 39.14 ± 12.7 years (ranging from 18 to 72 years). At the time of the study, only 40 patients (21.2%) were unvaccinated. Most of them presented with cough (n = 115, 67.6%), and acute viral syndrome symptoms (n = 115, 67.6%). The prevalence of COVID ocular involvement was estimated to be 20.6%. The most significant ocular manifestations, including eye discharge (*n* = 37, 19.6%), irritation (*n* = 31, 16.4%), epiphora (*n* = 30, 15.9%), and eye redness (*n* = 28, 14.8%), occurred within a week before COVID was detected. There were no correlations between ocular symptoms and comorbidities (*P* = .137), systemic symptoms (*P* = .133) or vaccination (*P* = .305).

Conclusion: Although most COVID patients had systemic symptoms, ocular involvement was only present in a minority and did not significantly affect ocular vision. We found no significant association between the presentation of ocular symptoms and comorbidities, systemic symptoms, or vaccination history in this study.

Keywords: COVID-19, ocular covid, online questionnaire
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Introduction

The coronavirus disease 2019 (COVID-19) is an emerging lower respiratory tract infectious disease, caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), an entity that the World Health Organization (WHO) has declared a global pandemic illness.[1,2]

There has been approximately 410 million cases of COVID-19 worldwide at the time of writing.[3] The relationship between SARS-CoV-2 infection and the eye remains controversial. The virus could occasionally be found in tears and conjunctival secretions in COVID-19 patients with or without conjunctivitis. Although the

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major transmission routes of SARS-CoV-2 are considered to be airborne droplets and close contact, ocular transmission has been reported with a great concern, particularly for the aerosol-generating procedures.[4-6]

Common clinical symptoms of COVID-19 infections include fever, cough, nasal obstruction, fatigue, headache, loss of taste or smell, nausea, vomiting, and diarrhea. Furthermore, 9.5 to 69.4% of patients with COVID-19[7-10] also manifest ocular symptoms such as eye redness, tearing or discharge, eye irritation or burning sensation, photophobia, or decreased vision.[11-13]

Realizing the prevalence and COVID-19 ocular characteristics may allow physicians to understand the infection more accurately and earlier in detection. The purpose of this study was to evaluate the characteristics of the COVID-19 ocular manifestations in Thailand.

Subjects/Materials and Methods

Ethical approval

This cross-sectional study was approved by the Human Research Ethics Committee of Thammasat University (No.221/2564) on 1 September 2021 in compliance with the Declaration of Helsinki. Participants were recruited between September and December 2021.

Participants

The study inclusion criteria were persons at least 18 years of age, testing positive RT-PCR for COVID-19 within the past 7 days, and registered to hospitalization or the home isolation program in the responsibility of Thammasat University Hospital, Thailand between September to November 2022. The exclusion criteria were moderate to severe COVID-19 conditions such as critical illness, unstable vital signs, oxygen therapy dependence, impaired daily personal care, inability to use a mobile web application, or history of any pre-existing ocular or systemic condition that, in the investigator's opinion, could confound the study results or interfere significantly with a patient's participation in the study.

Sample Size Calculation

The sample size was calculated using the formula

$$N = \frac{p_0 q_0 \left\{ z_{1-\alpha/2} + z_{1-\beta} \sqrt{\frac{p_1 q_1}{p_0 q_0}} \right\}^2}{(p_1 - p_0)^2}$$

$$q_0 = 1 - p_0$$

$$q_1 = 1 - p_1$$

where N = sample size for the study group, z = value of standard normal variate at 0.05 level of significance (1.96), p_0 = prevalence of COVID-19 infection (20%), p_1 = prevalence of ocular manifestations in COVID-19 (11.03%),[13] α = probability of type I error (0.05), β = probability of type II error (0.2). The final minimum sample size was calculated to be 136.

Data Collection

Following informed consent, the online questionnaire was answered voluntarily by anonymous respondents. Baseline characteristics including age, gender, locality, underlying disease, and pre-existing ocular condition were collected. History of COVID vaccination, clinical manifestation, and ocular involvement of COVID-19 infection was compiled. Incomplete questionnaire data were excluded from the statistical analysis.

Statistical Analysis

Binary and categorical response data (gender, region, underlying disease, baseline ocular condition, vaccination, COVID ocular severity grading and systemic symptoms) were shown as a percentage and proportions. Quantitative data (age) were presented as mean and standard deviation. McNemar test was used to assess the COVID ocular symptoms during the infectious period. Odds Ratio with 95% confidence interval was calculated to study the relationship between ocular severity symptoms and vaccination. *P*-value < .05 was considered to be statistically significant. All statistical analyses were performed using SPSS (Statistical Package of the Social Sciences, SPSS Inc., Chicago, IL) version 25.0 software.

Results

A total of 189 patients completed the survey questionnaire during the study period. 61 (32.3%) were males and 128 (67.7%) were females. The mean age of the patients was 39.14 ± 12.7 years (ranging from 18 to 72 years). Almost half of the participants lived in the Bangkok suburbs (46.5%). In the initial state of health, without any underlying disease (74.6%) and no prior eye drops administered (86.8%), only 21.2% of the individuals had been unvaccinated. The baseline characteristics of the participants are shown in Table 1.

Almost all of the participants exhibited coronavirus symptoms (89.9%), including fever (67.6%), upper respiratory tract symptoms; coughing (67.6%) and rhinorrhea (49.9%), and loss of smell (64.7%). Diarrhea is an infrequent symptom (20%). COVID-19 clinical manifestations are shown in Table 2.

Most COVID patients revealed asymptomatic eye conditions (79.4%). Meanwhile, eye discharge (19.6%, $P < .001$), irritation (16.4%, $P = .001$), epiphora (15.9%, $P < .001$), and eye redness (14.8%, $P = .002$) were all significant common ocular symptoms comparing to the pre-existing eye condition. Conversely, there was no statistical association between COVID infection and burning sensations (13.8%, $P = .122$) or blurred vision (11.1%, $P = .839$). Clinically, the ocular symptoms emerge within a week before COVID was detected (82.1%), as shown in Table 2-3, and presented in a mild severity, as demonstrated in Chart 1.

In this study, comorbidities [OR 1.65 (0.85-3.19) $P = .137$], vaccination [OR 2.26 (0.78-6.57) $P = .133$], and systemic symptoms [OR 0.69 (0.34-1.40) $P = .305$] are not associated with ocular involvement as additional information in Table 4.

Table 1: Baseline Characteristics

Baseline Characteristics			
Demographics			
Sex	Male	61 (32.3%)	
	Female	128 (67.7%)	
Age, year		39.14 ± 12.7	(range 18- 74)
Regional distribution			
Bangkok	47 (24.9%)		
Bangkok suburbs	88 (46.5%)		
Central region	18 (9.5%)		
Northern region	6 (3.2%)		
Northeastern region	25 (13.2%)		
Other areas	5 (2.6%)		
Underlying disease			
None	141 (74.6%)		
Hypertension	22 (11.6%)		
Diabetes	10 (5.3%)		
Arteriosclerosis	4 (2.2%)		
Other	38 (20.1%)		
Prior eye droplet medication			
None	164 (86.8%)		
Artificial tears	25 (12.2%)		
Other	4 (2.1%)		
Vaccination			
Unvaccinated	40 (21.2%)		
Vaccinated	149 (78.8%)		

Table 2: COVID-19 clinical manifestation

COVID-19 clinical manifestation		
Systemic symptoms		
None	19 (10.1%)	
Positive symptoms	170 (89.9%)	
Fever	115 (67.6%)	
Cough	115 (67.6%)	
Loss of smell	110 (64.7%)	
Rhinorrhea	84 (49.9%)	
Diarrhea	34 (20%)	
Other	7 (4.1%)	
Ocular involvement		
Positive symptoms	39 (20.6%)	
Eye discharge	37 (19.6%)	Mucous (n = 33, 89.19%), Yellowish (n = 4, 10.81%)
Irritation	31 (16.4%)	
Epiphora	30 (15.9%)	
Eye redness	28 (14.8%)	
Burning sensation	26 (13.8%)	
Blurring vision	21 (11.1%)	

Table 3: COVID-19 Ocular involvement

COVID-19 Ocular involvement			
Symptoms	**Pre-existing period**	**COVID period**	***P*-value**
Eye discharge	9 (4.8%)	37 (19.6%)	< .001*
Irritation	14 (7.4%)	31 (16.4%)	.001*
Epiphora	0 (0%)	30 (15.9%)	< .001*
Eye redness	15 (7.9%)	28 (14.8%)	.002*
Burning sensation	17 (9%)	26 (13.8%)	.122
Blurring vision	19 (10.1%)	21 (11.1%)	.839

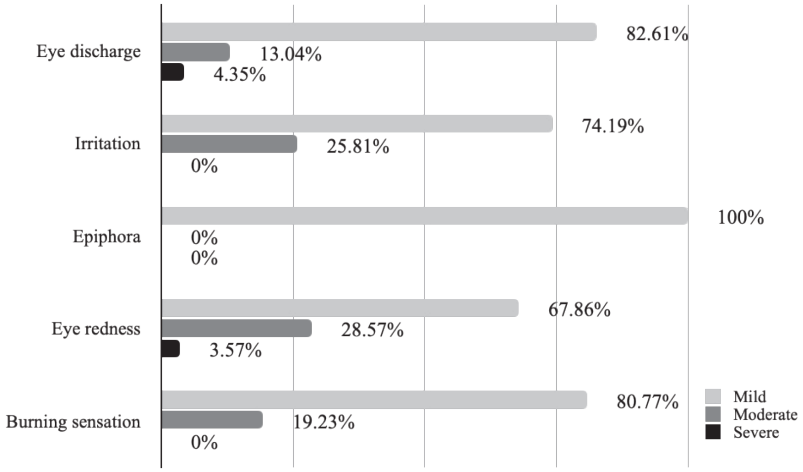

Chart 1: Severity of COVID-19 ocular symptoms

*McNemar test

Table 4: Correlations between variables and the ocular manifestation

Correlations between variables and the ocular manifestation		
	OR (95% CI)	***P*-value**
Comorbidities		
None		
Comorbidities	1.65 (0.85 - 3.19)	.137
Systemic symptoms		
None		
Positive symptoms	2.26 (0.78 - 6.57)	.133
Vaccination		
Unvaccinated		
Vaccinated	0.69 (0.34 - 1.40)	.305

Discussion

The coronavirus disease 2019 (COVID-19) is an emerging global pandemic infection that mainly affects the respiratory system. The main route of transmission is contaminated respiratory droplets and direct contact. Nevertheless, the ocular surface could be a susceptible exposure site consequence of Human angiotensin-converting enzyme 2 (ACE-2) receptors expression.[15-16] Teresa et al. reported that SARS-CoV-2 can be detected in tears and conjunctival secretions of patients with COVID-19, which is not associated with the positive ocular samples and ocular symptoms.[17] Kaya and Marlies et al. published that 7-16% of COVID-19 patients demonstrated a viral load in tears and conjunctival secretions, regardless of the presence of conjunctivitis or other ocular manifestations, that was higher than the range of 3-5% reported in a previous studies.[18-20]

According to the large systematic review, 38 studies with a total of 8,219 COVID-19 patients, documented that the prevalence of ocular manifestations was estimated to be 11.03%.[21] Meduri and colleagues, in their review, reported that conjunctival hyperemia occurred in 24.1%, tearing in 17.2%, and chemosis in 3.4% of patients.[22] In our study, the occurrence of symptomatic ocular COVID was about 20.6% with mild severity. The study result revealed that eye discharge (19.6%), irritation (16.4%), epiphora (15.9%), and eye redness (14.8%) were the most common ocular symptoms, occurring within a week of COVID detection. The other studies also found that viral conjunctivitis and chemosis were the initial presentations. The sensitivity of COVID-19 detection can be improved by paying attention to these signs, especially conjunctivitis.[21]

Similar to Nissar et al., there was no association between gender, comorbidities, and ocular involvement.[23] Furthermore, this study reported that systemic symptoms and vaccination were not associated as well.

Due to the methodological limitations of online questionnaires, interpretation bias from subjective self-evaluation was a consideration. This study was conducted in a target population with asymptomatic presentation and mild severity of COVID infection. Patients who are hospitalized with a serious condition would benefit from a physical examination rather than a questionnaire. However, an online assessment offers the advantages of literal distribution to the multicenter study scale, having flexibility and scalability, and allowing respondent anonymity. Furthermore, there is also potential fort integrating medical technology into "telemedicine" in order to reduce direct contact and disease transmission during the COVID pandemic.

Conclusion

Although most COVID patients had systemic symptoms, ocular involvement presented in a minority and did not significantly affect ocular vision. We found no significant association between the presentation of ocular symptoms and comorbidities, systemic symptoms, or vaccination history in this study.

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