

BRIEF REPORT

Open Access



Ocular symptoms in COVID-19 infection: a survey study

Matthew McHarg^{1,2}, Yujuan Wang¹, Mehmet Yakin^{1,3}, Alex Zeleny^{1,4}, Sonny Caplash⁵, H Nida Sen¹ and Shilpa Kodati^{1*}

Abstract

Background: Coronavirus disease 2019 (COVID-19) systemic symptoms and sequelae have been studied extensively, but less is known about the characterization, duration, and long-term sequelae of ocular symptoms associated with COVID-19 infection. The purpose of this study was to analyze the frequency, spectrum, and duration of ocular symptoms in participants with COVID-19 infection treated in inpatient and outpatient settings.

Methods: A retrospective electronic survey was distributed to NIH employees and the public who reported testing positive for SARS-CoV-2. The anonymous survey collected information on demographics, past ocular history, systemic COVID-19 symptoms, and ocular symptoms.

Results: A total of 229 (21.9% male and 78.1% female, mean age 42.5 ± 13.9) survey responses were included. Ocular symptoms were reported by 165 participants with a mean of 2.31 ± 2.42 symptoms. The most commonly reported ocular symptoms were light sensitivity (31.0%), itchy eyes (24.9%), tearing (24.9%), eye redness (24.5%), and eye pain (24.5%). Participants with ocular symptoms had a higher number of systemic symptoms compared to participants without ocular symptoms (mean 9.17 ± 4.19 vs 6.22 ± 3.63 ; OR: 1.21; 95% CI: 1.11 – 1.32; $p < 0.001$). Ocular symptoms were more common in those who reported a past ocular history compared to those who did not (81.8% vs 67.1%; OR: 2.17; 95% CI: 1.08 – 4.37; $p = 0.03$). Additionally, the onset of ocular symptoms occurred most frequently at the same time as systemic symptoms (47.5%), and 21.8% reported symptoms lasting ≥ 14 days.

Conclusions: Ocular surface-related symptoms are the most frequent ocular manifestations, and systemic disease severity is associated with the presence of ocular symptoms. Additionally, our results show that ocular symptoms can persist post-COVID-19 infection. Further work is needed to better understand ocular symptoms in COVID-19 and long-term sequelae.

Keywords: COVID-19, Survey study, Ocular surface, Infection, Inflammation

Background

A number of ocular manifestations have been reported in association with the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), including conjunctivitis, chemosis, and uveitis, amongst others [1–4]. Although reported rates of ocular symptoms have varied,

a recent meta-analysis by Inomata et al. reported that 11.2% of coronavirus disease 2019 (COVID-19) patients experienced some form of ocular manifestation [5]. Another meta-analysis of COVID-19 patients by Lofredo and colleagues reported the frequency of conjunctivitis, the most commonly described ocular manifestation of SARS-CoV-2 infection, as 5.9% [6, 7].

Currently, several theories exist regarding the pathogenesis of ocular symptoms associated with COVID-19 infection. Notably, the ocular surface has been implicated as a potential route of entry of SARS-CoV-2 virus

*Correspondence: Shilpa.Kodati@nih.gov

¹ National Eye Institute, National Institutes of Health, 10 Centre Drive, 10/10N248, Bethesda, MD, USA
Full list of author information is available at the end of the article

through the nasolacrimal system [8, 9]. Additionally, conjunctival expression of angiotensin-converting enzyme 2 (ACE2), which mediates viral entry into the host cell, and transmembrane serine protease 2 (TMPRSS2), which cleaves the virus’s spike (S) protein, may facilitate an ocular route of viral entry [10]. Although SARS-CoV-2 has also been detected via reverse transcription polymerase chain reaction (RT-PCR) on conjunctival swabs, evidence of spread via ocular secretions is still inconclusive [11, 12].

Despite these reports, more information is still needed on the frequency, timing, spectrum, and duration of SARS-CoV-2-associated ocular symptoms. Additionally, the majority of published reports describing ocular symptoms involve hospitalized patients, whereas comparatively less is known about those treated in the outpatient setting. Thus, the purpose of this study is to systematically characterize the range of ocular symptoms found in majority non-hospitalized individuals with COVID-19 infection.

Methods

A survey was developed using the online program Research Electronic Data Capture (REDCap), hosted within the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). REDCap is a secure, web-based application designed to support data capture for research studies; it was developed and is licensed by Vanderbilt University [13]. Responses were collected and managed using REDCap’s survey tools, and consulting support was provided by the Biomedical Translational Research Information System (BTRIS). Both NIDDK and BTRIS are part of the National Institutes of Health (NIH).

Our survey was designed to gather a large amount of information regarding ocular symptoms in COVID-19 infection. The study information was distributed to NIH employees who had tested positive for SARS-CoV-19, as well as the general public through social media and patient recruitment mailing lists. The survey queried participants about demographics, past ocular and medical history, details of their COVID-19 infection, and ocular symptoms. All responses were kept anonymous, and survey responses were collected from October 2020 through June 2021. In order to participate in the study, respondents were required to consent to completing the survey, confirm testing positive for SARS-CoV-2 via a polymerase chain reaction (PCR) test, and attest that they were 18 years of age or older. This study was approved as exempt by the NIH Office of IRB Operations, and patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this project.

Only complete responses were included for analysis. For statistical analyses, SPSS v.17.0 statistical software for Windows (SPSS Inc., Chicago, IL) was used. For descriptive statistics, continuous variables are presented as means ± standard deviations, and categorical variables are presented as frequencies and proportions. Multi-variable logistic regression models were used to identify significant predictors of clinical symptoms adjusted by age, gender and race. Comparisons of continuous variables between two variables were done by student t-test for normally distributed variables. For variables without normal distribution, Mann–Whitney U test was used for comparisons between two independent variables. A two-tailed *p* value of <0.05 was considered significant.

Results

Following exclusion of ineligible participants and incomplete responses, 229 (21.9% male and 78.1% female, mean age 42.5 ± 13.9 years) complete survey responses were included for analysis from both hospitalized (10.0%) and non-hospitalized (90.0%) respondents (Table 1).

NIH employees and health-care workers accounted for 32.3% and 37.6% of responses, respectively, and 30.1% were tested as part of a healthcare employee testing program. Most participants resided in the United States (94.3%). A total of 77 patients (33.6%) reported a past ocular history (Table 2), including most frequently

Table 1 Participant demographics. Significant differences (*p* < 0.05) between hospitalized and non-hospitalized participant demographics are displayed in bold text

Demographics	Hospitalized (n = 23)	Non-hospitalized (n = 206)	Total (n = 229)
Age (mean ± SD)	49.1 ± 15.8	41.8 ± 13.6	42.5 ± 13.9
Gender			
Female	15	163	178 (78.1%)
Male	8	42	50 (21.9%)
Unknown	0	1	1 (0.6%)
Race/Ethnicity			
White non-Hispanic	16	142	158 (69.0%)
Black	1	24	25 (10.9%)
Asian	4	18	22 (9.6%)
White Hispanic	0	13	13 (5.7%)
Other	2	9	11 (4.8%)
Country of residence			
US	20	196	216 (94.3%)
Other	3	10	13 (5.7%)
Employment			
Healthcare worker	4 (17.4%)	82 (39.8%)	86 (37.6%)
NIH employee	1 (4.3%)	73 (35.4%)	74 (32.3%)

Table 2 Past ocular history reported by survey participants

Past Ocular History	Total (n = 229)
Conjunctivitis	26 (11.4%)
Dry eye	25 (10.9%)
Other	19 (8.3%)
Cataract	12 (5.2%)
Allergic Eye Disease	7 (3.1%)
Strabismus	6 (2.6%)
Eye Injury	3 (1.3%)
Double vision	2 (0.9%)
Retinal detachment	2 (0.9%)
Macular degeneration	2 (0.9%)
Uveitis	2 (0.9%)
Sudden irreversible vision loss	1 (0.4%)
Thyroid eye disease	1 (0.4%)
Blindness	0
Color Blindness	0
Glaucoma	0
Sudden reversible vision loss	0
Diabetic retinopathy	0

conjunctivitis (11.4%) and dry eyes (10.9%). Further, 27 participants (11.8%) reported using eyedrops including artificial tears, lubricating ointments, and/or anti-allergy drops before the onset of their symptoms.

All hospitalized participants (mean number of systemic symptoms: 10.00 ± 4.45) and 98.5% of non-hospitalized participants (mean number: 8.16 ± 4.19) experienced at least one COVID-19 associated systemic symptom. When separated by gender, the number of reported systemic symptoms was significantly higher in females than males (8.69 ± 4.39 vs 7.20 ± 3.49 , respectively; $p = 0.03$).

Ocular symptoms were reported by 165 (72.1%) participants (mean number of ocular symptoms per participant: 2.31 ± 2.42 ; range 0–11). The most frequently reported ocular symptoms were light sensitivity ($n = 71$, 31.0% of all respondents), itchy eyes ($n = 57$, 24.9%), tearing ($n = 57$, 24.9%), eye redness ($n = 56$, 24.5%), eye pain ($n = 56$, 24.5%), blurred vision ($n = 52$, 22.7%), and foreign body sensation ($n = 43$, 18.8%). Ocular symptoms were predominantly bilateral (90.9%). A summary of ocular symptom data can be found in Table 3.

When separated by inpatient and outpatient settings, ocular symptoms were reported in 20 (87.0%) hospitalized respondents compared to 145 (70.4%) non-hospitalized respondents (OR: 3.50; 95% CI: 0.94 – 13.02; $p = 0.06$). The mean number of ocular symptoms per respondent was also significantly greater in hospitalized participants than in their non-hospitalized counterparts (3.91 ± 3.09 vs 2.14 ± 2.28 , respectively; $p = 0.01$). Lastly, ocular symptoms were more common in those who

Table 3 Ocular symptoms reported by survey participants. Significant differences ($p < 0.05$) between hospitalized and non-hospitalized ocular symptoms are displayed in bold text

Ocular symptoms	Hospitalized (n = 23)	Non-hospitalized (n = 206)	Total (n = 229)
Light sensitivity	12 (52.2%)	59 (28.6%)	71 (31.0%)
Tearing	10 (43.5%)	47 (22.8%)	57 (24.9%)
Itchy eyes	6 (26.1%)	51 (24.8%)	57 (24.9%)
Redness	10 (43.5%)	46 (22.3%)	56 (24.5%)
Pain	6 (26.1%)	50 (24.3%)	56 (24.5%)
Blurred vision	10 (43.5%)	42 (20.4%)	52 (22.7%)
Foreign body sensation	5 (21.7%)	38 (18.4%)	43 (18.8%)
Mucous discharge	8 (34.8%)	33 (16.0%)	41 (17.9%)
Floaters	7 (30.4%)	29 (14.1%)	36 (15.7%)
Flashes of light	6 (26.1%)	17 (8.3%)	23 (10.0%)
Eyelid swelling	3 (13.0%)	15 (7.3%)	18 (7.9%)
Blind spots	3 (13.0%)	7 (3.4%)	10 (4.4%)
Double vision	4 (17.4%)	6 (2.9%)	10 (4.4%)

reported a past ocular history compared to those who did not (81.8% vs 67.1%; OR: 2.17; 95% CI: 1.08 – 4.37; $p = 0.03$).

The association between ocular and systemic symptoms was examined in-depth (Tables 4 and 5). Systemic disease severity was associated with the presence of ocular symptoms, as participants with ocular symptoms had a higher number of systemic symptoms compared to participants without ocular symptoms (mean 9.17 ± 4.19 compared to 6.22 ± 3.63 ; OR: 1.21; 95% CI: 1.11 – 1.32; $p < 0.001$). Additionally, the onset of ocular symptoms occurred most frequently at the same time as systemic symptoms (47.5%) when compared to before (17.5%) and after systemic symptoms (35.0%).

There was no significant difference in the number of respondents who reported ≥ 1 ocular symptom when the responses were divided into age groups (18–29 years, 30–49 years, ≥ 50 years). When specific eye symptoms were analyzed, however, foreign body sensation was reported significantly more frequently in the ≥ 50 age group (OR: 4.81; 95% CI: 1.47 – 15.74; $p = 0.01$), and blurred vision was significantly common in 30 – 49 and ≥ 50 age groups (OR: 4.85; 95% CI: 1.46 – 16.08; $p = 0.01$ and OR: 7.99; 95% CI: 2.30 – 27.80; $p = 0.001$ respectively).

Respondents were also asked about whether their ocular symptoms were ongoing or had resolved at the time of their responses. Of the participants who reported resolved symptoms, the mean duration of symptoms was 16.2 days ± 50.6 . A total of 31 (18.8%) respondents reported ongoing ocular symptoms with

Table 4 Relationship between systemic symptoms and any ocular symptoms adjusted for age, gender, and race. Significant results ($p < 0.05$) are displayed in bold text

Systemic Symptom	Symptom present?	Any ocular symptom	OR*	95% CI*	P-value*
Measured fever > 100.4 F	No	94 (66.2%)	1		
	Yes	71 (81.6%)	2.31	1.18 – 4.52	0.02
Subjective fever	No	95 (69.9%)	1		
	Yes	70 (75.3%)	1.32	0.71 – 2.43	0.38
Chills	No	65 (62.5%)	1		
	Yes	100 (80.0%)	2.27	1.23 – 4.19	0.01
Muscle aches	No	41 (57.7%)	1		
	Yes	124 (78.5%)	2.46	1.32 – 4.59	0.01
Joint pain	No	86 (64.7%)	1		
	Yes	79 (82.3%)	2.28	1.17 – 4.42	0.02
Runny nose	No	78 (65.0%)	1		
	Yes	87 (79.8%)	2.14	1.14 – 4.01	0.02
Sore throat	No	88 (68.2%)	1		
	Yes	77 (77.0%)	1.65	0.89 – 3.06	0.12
Cough	No	49 (62.0%)	1		
	Yes	116 (77.3%)	1.94	1.05 – 3.60	0.03
Shortness of breath	No	99 (69.2%)	1		
	Yes	66 (76.7%)	1.47	0.77 – 2.79	0.24
Wheezing	No	131 (68.6%)	1		
	Yes	34 (89.5%)	4.25	1.39 – 13.01	0.01
Chest pain	No	112 (65.5%)	1		
	Yes	53 (91.4%)	5.81	2.13 – 15.84	0.001
Fatigue/Tiredness	No	29 (56.9%)	1		
	Yes	136 (76.4%)	2.48	1.23 – 4.97	0.01
Nausea/Vomiting	No	113 (68.5%)	1		
	Yes	52 (81.3%)	1.71	0.82 – 3.56	0.15
Headache	No	46 (63.9%)	1		
	Yes	119 (75.8%)	1.80	0.95 – 3.40	0.07
Abdominal pain	No	135 (68.2%)	1		
	Yes	30 (96.8%)	13.16	1.73 – 99.92	0.01
Diarrhea	No	103 (67.3%)	1		
	Yes	62 (81.6%)	2.26	1.13 – 4.55	0.02
Loss of taste	No	67 (67.0%)	1		
	Yes	98 (76.0%)	1.50	0.82 – 2.73	0.19
Loss of smell	No	62 (66.7%)	1		
	Yes	103 (75.7%)	1.55	0.85 – 2.83	0.15
Other	No	129 (68.3%)	1		
	Yes	36 (90.0%)	4.07	1.34 – 12.38	0.01

*Adjusted for age, gender and race

a mean duration of 73.6 days (± 104.6). Amongst all respondents who endorsed ocular symptoms, both resolved and ongoing, 36 (21.8%) had eye symptoms lasting ≥ 14 days (range 14–400 days; mean 2.28 ± 1.86 symptoms per participant). Of these, 3 participants were hospitalized and 33 were non-hospitalized. The most frequently reported ocular symptoms

lasting ≥ 14 days were blurred vision ($n = 14$, 8.4% of respondents with ocular symptoms), floaters ($n = 9$, 5.5%), eye redness ($n = 8$, 5.5%), tearing ($n = 8$, 5.5%), and sensitivity to light ($n = 8$, 5.5%). All 13 ocular symptoms were reported at least once, and each ocular symptom had at least one respondent who experienced persistent symptoms for ≥ 14 days.

Table 5 Relationship between any ocular symptoms and age, gender, and race

	OR	95% CI	P-value
Age	1.01	0.99—1.03	0.37
Gender			
Male	1		
Female	1.78	0.90—3.51	0.10
Race / ethnicity			
White non-Hispanic	1		
White Hispanic	0.62	0.19—2.02	0.43
Black	1.89	0.61—5.88	0.27
Asian	0.50	0.20—1.28	0.15
Others	1.12	0.28—4.50	0.87

Notably, only 22 (13.3%) of respondents with ocular symptoms sought medical attention by an eye care professional (ophthalmologist or optometrist). Of those participants who sought care, 9 out of 22 (40.9%) respondents had their eye symptoms attributed to COVID-19 infection by their eye care professional.

Discussion

Our results demonstrate several points of interest, including 1) ocular surface related symptoms are the most frequently reported ocular symptoms in COVID-19 infection; 2) ocular symptoms are more frequent in those with a reported past ocular history; 3) systemic disease severity is associated with the presence of ocular symptoms; and 4) a proportion of participants reported post-COVID-19 persistent ocular symptoms.

In large-scale studies, the reported prevalence of ocular findings in COVID-19 infection have varied from as low as 1.4% to as high as 11.2% [5, 14, 15]. However, Inomata and colleagues suggested that these numbers are likely an underestimation, as individuals with COVID-19 have a range of manifestations and may be unlikely to seek out ophthalmic evaluation when other life-threatening symptoms are present. The most frequently observed signs in a meta-analysis by La Distia Nora et al. were epiphora, conjunctival injection, and chemosis, which are commonly seen in other forms of viral conjunctivitis [16]. Other reported ocular findings have included both anterior and posterior segment findings such as conjunctivitis, uveitis, acute macular neuroretinopathy, and retinopathy [17, 18]. Notably, ocular manifestations have occasionally been described as the sole or initial presentation of SARS-CoV-2 infection [19–21]. The majority of large series studies that investigate ocular manifestations of COVID-19 are in hospitalized patients, and differentiating these

manifestations from factors related to hospitalization rather than the infection itself, especially with intensive care, can be challenging. Thus, our study provides insight into ocular symptoms experienced by COVID patients who were—in large part—not hospitalized (90.0%).

Although survey and cross-sectional studies have reported varying frequencies of ocular symptoms, current literature points towards a predominance of ocular surface symptoms when eye symptoms are present. A recent meta-analysis by Soltani et al. found that the most prevalent ocular symptoms were dry eyes (23.8%) and eye pain (10.3%) [22]. Similarly, Nasiri et al., in their meta-analysis, found the most common ocular manifestations to be dry eyes/foreign body sensation (16.0%), redness (13.3%), tearing (12.8%), itching (12.6%), and eye pain (9.8%) [23]. Although varied, these analyses are largely consistent with the ocular symptoms most commonly reported in our study, including light sensitivity (31.0%), itchy eyes (24.9%), tearing (24.9%), and eye redness/pain (24.5%).

Corneal and conjunctival expression of ACE2 receptor, a known entry mechanism of the SARS-CoV-2, has been postulated as a potential mechanism for direct viral invasion of the ocular surface and subsequent ocular manifestations [10, 24]. Additionally, Zhong and colleagues revealed a pooled positivity rate of 3.9% from conjunctival swabs [16]; however, there are numerous studies that have reported patients with positive conjunctival swabs but no ocular symptoms, and vice versa [1, 12, 25]. Further, a review by Douglas and colleagues concluded there is no clear relationship between conjunctival titers and transmissibility [2]. Overall, current research indicates that the relationship between PCR positivity in conjunctival swabs, transmission, and ocular symptoms remains unclear.

Reports have also found that patients with severe disease were more likely to have associated ocular manifestations, presumably due to a higher viral load leading to disseminated disease [16, 26]. Our study yielded similar results, showing that participants with ocular manifestations had 9.17 ± 4.19 systemic symptoms, while those without ocular symptoms had 6.22 ± 3.63 systemic symptoms ($p < 0.001$).

The majority of participants in our study (47.5%) reported the onset of ocular symptoms at the same time as systemic symptoms. However, 17.5% of reported ocular symptoms presented prior to the onset of systemic symptoms. These results are consistent with La Distia Nora and colleagues' study and the meta-analysis by Inomata et al., who reported prodromal ocular symptoms in 28% and 12.5% of cases, respectively [5, 15]. These findings highlight the need for

ophthalmologists to maintain a high degree of suspicion when evaluating patients with ocular surface complaints during the COVID-19 pandemic.

There is a paucity of data in the literature regarding ocular symptoms associated with “long-haul” COVID-19 infection. A significant proportion of participants with ocular symptoms (21.8%) in our study reported eye symptoms lasting ≥ 14 days, including most frequently blurred vision, floaters, eye redness, tearing, and sensitivity to light. Pardhan and colleagues reported eye symptoms lasting ≥ 14 days in 20% of their cohort [27], and Vallejo-Garcia et al. observed persistent conjunctivitis in 9.4% of their patients with a mean follow up time of 6 weeks after the initial positive COVID-19 test [28]. Notably, in the study by Vallejo-Garcia and colleagues, conjunctival swabs were negative in all patients with persistent ocular symptoms, which may suggest that the ocular symptoms are not the result of active infection. Other than these few reports, there is little data regarding post-COVID-19 infection ocular symptoms, and potential mechanisms are still being investigated. Indeed, it remains unclear whether the mechanisms of systemic “long-haul” COVID-19 infection, which have been attributed viral persistence in ACE2-expressing organ systems, autoimmunity due to cryptic antigens and viral mimicry, and persistent inflammation due to the altered cytokine environment and persistence of pro-inflammatory immune cells, can explain the persistence of ocular symptoms [29].

This study has several limitations: As with any survey study, there is unavoidable recall bias and there are varying levels of symptom awareness between survey participants. There is also likely an inclusion bias towards respondents experiencing eye symptoms, as this survey was distributed by the National Eye Institute. This bias at least partially accounts for the high frequency of ocular symptoms in our study (72.1%). Another potential limitation is that our study reported ocular *symptoms* of COVID-19 experienced by patients, not *diagnoses* since the respondents were not examined by an ophthalmologist at the time of survey completion. Lastly, the results of this study would have been strengthened by a larger and more representative sample size.

In conclusion, our results show that ocular surface-related symptoms were more common and vision-affecting symptoms were rare. The majority of participants reported the onset of ocular symptoms at the same time as systemic symptoms, and over a fifth of our respondents reported ocular symptoms lasting ≥ 14 days in duration. As vaccination rates increase, hospitalization rates fall, and outpatient cases rise; we believe these results are critical to the understanding of COVID-19 and its ocular manifestations, particularly in outpatient settings.

Overall, further research is needed to fully comprehend the pathophysiology and sequelae of ocular symptoms associated with COVID-19 infection.

Abbreviations

SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2; COVID-19: Coronavirus disease 2019; ACE2: Angiotensin-converting enzyme; TMPRSS2: Transmembrane serine protease 2; RT-PCR: Reverse transcription polymerase chain reaction; REDCAP: Research Electronic Data Capture; NIDDK: National Institute of Diabetes and Digestive and Kidney Diseases; BTRIS: Biomedical Translational Research Information System; NIH: National Institutes of Health.

Acknowledgements

The authors would like to thank Michael Ring and Kerry Goetz for their assistance with the creation and implementation of the REDCap survey.

Authors' contributions

M.M. and Y.W. made substantial contributions to the conception, design, and acquisition of survey data. M.Y., M.M., and Y.W. analyzed survey data. M.Y. prepared Tables 1-5. M.M., A.Z., and S.C. made major contributions to writing and revising this manuscript. S.K. and H.N.S. made substantial contributions towards editing and reviewing the manuscript. All authors read, reviewed, and approved the final manuscript.

Funding

Open Access funding provided by the National Institutes of Health (NIH). Funding was provided by the NEI Intramural Research Program.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Author details

¹National Eye Institute, National Institutes of Health, 10 Centre Drive, 10/10N248, Bethesda, MD, USA. ²George Washington University School of Medicine and Health Sciences, Washington, DC, USA. ³Department of Ophthalmology, University of Health Sciences, Ankara Training and Research Hospital, Ankara, Turkey. ⁴Georgetown University School of Medicine, Washington, DC, USA. ⁵Department of Ophthalmology, University of Pittsburgh Medical Center, Pittsburgh, PA, USA.

Received: 28 May 2022 Accepted: 28 November 2022

Published online: 20 December 2022

References

1. Wu P, Duan F, Luo C et al (2020) Characteristics of Ocular Findings of Patients With Coronavirus Disease 2019 (COVID-19) in Hubei Province, China. *JAMA Ophthalmol* 138(5):575–578
2. Douglas KAA, Douglas VP, Moschos MM (2020) Ocular Manifestations of COVID-19 (SARS-CoV-2): A Critical Review of Current Literature. *In Vivo* 34(3 Suppl):1619–1628
3. Meduri A, Oliverio GW, Mancuso G et al (2020) Ocular surface manifestation of COVID-19 and tear film analysis. *Sci Rep* 10(1):20178

4. Chen L, Deng C, Chen X et al (2020) Ocular manifestations and clinical characteristics of 535 cases of COVID-19 in Wuhan, China: a cross-sectional study. *Acta Ophthalmol* 98(8):e951–e959
5. Inomata T, Kitazawa K, Kuno T et al (2020) Clinical and Prodromal Ocular Symptoms in Coronavirus Disease: A Systematic Review and Meta-Analysis. *Invest Ophthalmol Vis Sci* 61(10):29
6. Loffredo L, Fallarino A, Parainfini A et al (2021) Different rates of conjunctivitis in COVID-19 eastern and western hospitalized patients: a meta-analysis. *Intern Emerg Med* 17(3):925–928
7. Kitazawa K, Deinhardt-Emmer S, Inomata T et al (2021) The transmission of SARS-CoV-2 infection on the ocular surface and prevention strategies. *Cells* 10(4):796
8. Hu Y, Chen T, Liu M et al (2020) Positive detection of SARS-CoV-2 combined HSV1 and HHV6B virus nucleic acid in tear and conjunctival secretions of a non-conjunctivitis COVID-19 patient with obstruction of common lacrimal duct. *Acta Ophthalmol* 98(8):859–863
9. Collin J, Queen R, Zerti D et al (2021) Co-expression of SARS-CoV-2 entry genes in the superficial adult human conjunctival, limbal and corneal epithelium suggests an additional route of entry via the ocular surface. *Ocul Surf* 19:190–200
10. Zhou L, Xu Z, Castiglione GM et al (2020) ACE2 and TMPRSS2 are expressed on the human ocular surface, suggesting susceptibility to SARS-CoV-2 infection. *Ocul Surf* 18(4):537–544
11. Ho D, Low R, Tong L et al (2020) COVID-19 and the ocular surface: a review of transmission and manifestations. *Ocul Immunol Inflamm* 28(5):726–734
12. Dockery DM, Rowe SG, Murphy MA et al (2020) The ocular manifestations and transmission of COVID-19: recommendations for prevention. *J Emerg Med* 59(1):137–140
13. Harris PA, Taylor R, Thielke R et al (2009) Research electronic data capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform* 42(2):377–381
14. Wang D, Hu B, Hu C et al (2020) Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA* 323(11):1061–1069
15. La Distia NR, Putera I, Khalisha DF et al (2020) Are eyes the windows to COVID-19? Systematic review and meta-analysis. *BMJ Open Ophthalmol* 5(1):e000563
16. Zhong Y, Wang K, Zhu Y et al (2021) Ocular manifestations in COVID-19 patients: a systematic review and meta-analysis. *Travel Med Infect Dis* 44:102191
17. David JA, Fivgas GD (2021) Acute macular neuroretinopathy associated with COVID-19 infection. *Am J Ophthalmol Case Rep* 24:101232
18. Zhang Y, Stewart JM (2021) Retinal and choroidal manifestations of COVID-19. *Curr Opin Ophthalmol* 32(6):536–540
19. Scalinci SZ, Trovato BE (2020) Conjunctivitis can be the only presenting sign and symptom of COVID-19. *IDCases* 20:e00774
20. Cheema M, Aghazadeh H, Nazarali S et al (2020) Keratoconjunctivitis as the initial medical presentation of the novel coronavirus disease 2019 (COVID-19). *Can J Ophthalmol* 55(4):e125–e129
21. Ozturker ZK (2021) Conjunctivitis as sole symptom of COVID-19: a case report and review of literature. *Eur J Ophthalmol* 31(2):NP161–NP6
22. Soltani S, Zandi M, Ahmadi SE et al (2022) Pooled prevalence estimate of ocular manifestations in COVID-19 patients: a systematic review and meta-analysis. *Iran J Med Sci* 47(1):2–14
23. Nasiri N, Sharifi H, Bazrafshan A et al (2021) Ocular manifestations of COVID-19: a systematic review and meta-analysis. *J Ophthalmic Vis Res* 16(1):103–112
24. Napoli PE, Nioi M, d'Aloja E et al (2020) The ocular surface and the coronavirus disease 2019: does a dual 'ocular route' exist? *J Clin Med* 9(5):1269
25. Rodriguez-Ares T, Lamas-Francis D, Trevino M et al (2021) SARS-CoV-2 in conjunctiva and tears and ocular symptoms of patients with COVID-19. *Vision (Basel)* 5(4):51
26. Jevnikar K, Jaki Mekjivic P, Vidovic Valentincic N et al (2021) An update on COVID-19 related ophthalmic manifestations. *Ocul Immunol Inflamm* 29(4):684–689
27. Pardhan S, Vaughan M, Zhang J et al (2020) Sore eyes as the most significant ocular symptom experienced by people with COVID-19: a comparison between pre-COVID-19 and during COVID-19 states. *BMJ Open Ophthalmol* 5(1):e000632
28. Vallejo-García JL, Balia L, Raimondi R et al (2021) Conjunctivitis as a sign of persistent SARS-COV-2 infection? An observational study and report of late symptoms. *Eur J Ophthalmol* 32(2):11206721211056594
29. Mehandru S, Merad M (2022) Pathological sequelae of long-haul COVID. *Nat Immunol* 23(2):194–202

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Submit your manuscript to a SpringerOpen® journal and benefit from:

- Convenient online submission
- Rigorous peer review
- Open access: articles freely available online
- High visibility within the field
- Retaining the copyright to your article

Submit your next manuscript at ► [springeropen.com](https://www.springeropen.com)
