

Eyes Have It: From COVID-19 Perspective

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Keywords: Adverse drug reactions, COVID-19, Emergency department, Eyecare, Pharmacovigilance, Trigger tool.

Indian Journal of Critical Care Medicine (2020); 10.5005/jp-journals-10071-23644

Sir,

The “2019 novel coronavirus disease (COVID-19)”, due to the infection of “severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2)” has emerged as the most discussed topic worldwide. As of now globally it has caused 4,338,658 cases with a fatality rate of 6.8% (WHO, May 15, 2020). Medical professionals accounted for about 20% of the United States and 9% of Italy’s total COVID-19 cases.¹ Three ophthalmologists from Wuhan Central Hospital have been fallen prey in line of duty, and Dr Guangfa Wang, a pulmonologist, was reported to afflict by SARS-CoV-2 through vulnerable ocular exposure.² These reports have amplified concerns about the course of dissemination.

The major source for COVID-19 infection is aerosol-generating procedures and direct contact. However, the oculo-pathogenic potential of human coronaviruses, and the role of ocular surface for transmission, and are not well addressed.

The SARS-CoV-2, a *Beta coronavirus* is transmitted through the angiotensin-converting enzyme 2 (ACE2) receptor, expressed in the cornea, conjunctiva,³ retina, and aqueous.⁴ The abundance of ACE2 receptors on the ocular surface makes them a prospective target of COVID-19. However, the accumulation of SARS-CoV-2 in ophthalmic secretions remains unclear. Probably due to direct inoculation by the aerosolized viral particles, transmission from the nasopharynx through the nasolacrimal duct.

In animal studies, coronaviruses have been associated with anterior uveitis, retinitis, vasculitis, and optic neuritis.⁵ Seventeen percent of human coronavirus NL 63 (HCoV-NL63) are found to be associated with conjunctivitis.¹

Around “0.8%” of “1,099” COVID-19 patients in China had reported conjunctival congestion.¹ Another recent case series also stated that “31.6%” of the COVID-19 hospitalized patients developed ocular symptoms comprising conjunctival hyperemia, chemosis, and epiphora. The reverse-transcriptase polymerase chain reaction (RT-PCR) for SARS-CoV-2 from the conjunctival swab along with the nasopharyngeal swabs had positive results in “16.7%” of them. The patients with ocular symptoms had a higher total leukocyte count, C-reactive protein, procalcitonin, and lactate dehydrogenase compared with patients without any signs of ophthalmological complications.⁶

Ophthalmology examination findings are consistent with follicular conjunctivitis of the bulbar conjunctiva, a follicular reaction involving the palpebral conjunctiva, watery discharge, and mild eyelid edema.¹ Isolated chemosis may indicate third-spacing in a severely ill patient. The ocular manifestations of COVID-19 have been described in three original studies and a few case reports (Table 1) to date. There is no reporting of diplopia, keratitis,

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How to cite this article: Sarkar S, Khanna P. Eyes Have It: From COVID-19 Perspective. *Indian J Crit Care Med* 2020;24(11):1139–1140.

Source of support: Nil

Conflict of interest: None

subconjunctival hemorrhage, and pseudomembrane formation in COVID-19 patients.

About one-third of hospitalized COVID-19 patients require intensive care support. The importance of eye care in these severely ill patients is paramount. Impaired blinking reflex causes drying of ocular surface which leads to the breakdown of corneal epithelium, thereby resulting in exposure keratopathy. Subsequent contamination from the respiratory secretions, and venous stasis, and conjunctival edema due to intermittent positive-pressure ventilation aggravate the situation.

Ting et al.⁷ have reported a case of the white cornea with presumed infection in a severely ill patient of COVID-19. Ensuring eye care through taping, use of the moist chamber, frost suture, 1% chloramphenicol ointment, 6–8 hourly checking of eyes, avoidance of aspiration of secretion over the face if the eyes are not covered, and early detection of the dull cornea may be useful to prevent this.⁷ Thus, incorporation of prevention, identification, and treatment of ocular complications as a component of the critical care bundle for COVID-19 is the need of the hour.

In the absence of significant pain, dimness of vision, patients can be treated with periodic application of cold compresses, preservative-free artificial tears, and lubricating ocular ointment. The use of topical antibiotics may be considered for preventing the bacterial superinfection depending on symptoms and customized risk factors (e.g., contact lens user).

Currently, antiviral, antimalarial, antiparasitic drugs, and other therapeutic agents, particularly targeted to prevent the “cytokine storm” associated in the critical cases, are being evaluated under controlled clinical settings for potential adverse interactions with other therapeutic agents and ocular toxicity (Table 2).

The refractory non-infective uveitis patients may require systemic immunosuppression. In the current scenario before starting systemic immunosuppression, screening for SARS-CoV-2

Table 1: Ophthalmological manifestations in COVID-19²

Study	Type	City	Key point	Link
1. Zhou et al.	Retrospective cohort study (n = 67)	Wuhan	SARS-CoV-2 detected in the conjunctival sac of patients with COVID-19.	https://doi.org/10.1101/2020.02.11.20021956
2. Sun et al.	Cross-sectional study (n = 102)	Wuhan	Nosocomial infection of SARS-CoV-2 through the eyes is a potential route.	https://doi.org/10.1101/2020.02.26.20027938
3. Xia et al.	Prospective case series study (n = 30)	Hangzhou	SARS-CoV-2 detected in the tears and conjunctival secretions of COVID-19 patients with conjunctivitis.	https://doi.org/10.1002/jmv.25725
4. Casalino et al.	Case report	Milan	A patient of COVID-19 presenting with unilateral conjunctivitis in Italy.	https://doi.org/10.1038/s41433-020-0909-x
5. Li et al.	Case series (n = 4)	Wuhan	Healthcare workers with COVID-19 presented with conjunctivitis.	https://doi.org/10.3760/cma.j.issn.2095-0160.2020.0002
6. Li et al.	Case series (n = 2)	Wuhan	Conjunctivitis as the first symptom in COVID-19 patients.	https://doi.org/10.3760/cma.j.issn.115989-20200303-00133
7. Ye et al.	Case series (n = 30)	Wuhan	Three cases of binocular conjunctivitis reported in patients with neuropathic corneal pain (NCP) and positive viral nucleic acid were detected in the conjunctiva sacs of 2 of other 27 NCP patients.	https://doi.org/10.3760/cma.j.cn112142-20200214-00063

Table 2: Ocular side effects of different trial drugs for COVID-19

Drugs	Ocular side effects	Toxic dosage
Hydroxychloroquine	Vortex keratopathy, maculopathy	>6.5 mg/kg/day with normal renal function
Ivermectin	Foreign body sensation, eyelid edema, anterior uveitis, blurred vision, conjunctival hemorrhage	>200 µg/kg
Tocilizumab	Retinopathy	>8 mg/kg
Ritonavir/lopinavir	Blurring of vision, toxic epidermal necrolysis	>800 mg/200 mg twice daily
Favipiravir	Blurring of vision, ocular pain, toxic epidermal necrolysis, Stevens–Johnson syndrome	Human data not available
Remdesivir	Safety and efficacy not established	Human data not available
Methylprednisolone	Ocular hypertension, posterior subcapsular cataract, open-angle glaucoma	>10 mg/day

may be beneficial. Management of COVID-19 patients with systemic immunosuppression is a challenging task, and the use of systemic corticosteroids in SARS-CoV-2 positive patients is still debatable. However, individualized treatment by a multidisciplinary approach comprising rheumatologists, ophthalmologists, and intensivists is necessary.

In conclusion, ocular surface infection is a potentially dangerous route of transmission, and healthcare professionals should be cautious in this regard. Further research on ophthalmological manifestation, viral transmission through ocular secretions, long-term complications of these patients is the need of the hour.

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