

Coronavirus and ophthalmology: What do we know and way forward

Coronavirus (CoV) outbreak is not a new phenomenon affecting human life. In 2003, it was severe acute respiratory syndrome coronavirus (SARS-CoV), which affected 8,422 individuals and resulted in 916 deaths globally.^[1] Later it was Middle East respiratory syndrome coronavirus (MERS-CoV) outbreak first identified in Saudi Arabia and Jordan in 2012, which infected 2,499 individuals and caused 858 deaths.^[2] More recently, in December 2019, a new CoV outbreak, known as severe acute respiratory syndrome coronavirus-2 (SARS-Cov-2), occurred in Wuhan in the Hubei province of China, which was declared as a pandemic by the World Health Organization (WHO).^[3,4]

By March 31, 2020, it had affected nearly a million individuals globally.^[4]

CoVs are also known to cause ocular infections in animals, such as conjunctivitis, anterior uveitis, retinitis, and optic neuritis.^[5] However, there are no reports on ocular involvement in humans infected with SARS-CoV or MERS-CoV, although polymerase chain reaction on tears from patients with SARS-CoV infection demonstrated the presence of virus.^[6] Two recent studies have reported on the ocular involvement in SARS-Cov-2.^[7,8] Guan W described the data obtained from 1,099 patients treated in 552 hospitals in 30 provinces of China. They included 926 non-severe cases and 173 severe cases, and conjunctival congestion was seen in 9 (0.8%) cases, 5 in non-severe cases (0.5%) and

4 in severe cases (2.3%).^[7] Similarly, Wu Ping *et al.* examined 38 patients in Hubei province and found ocular manifestation in 12 (31.6%) patients, which included conjunctivitis, conjunctival hyperemia, chemosis, epiphora, or increased secretions.^[8] Among 12 patients, 4 were non-severe cases and 8 were severe or critical cases.^[8] There were only 2 patients who showed positive for SARS-CoV-2, both in conjunctival and nasopharyngeal swabs.^[8] The univariate analysis also showed that patients with ocular symptoms were more likely to have higher white blood cell counts and neutrophils, procalcitonin, C-reactive protein, and lactate dehydrogenase.^[8] Both of these studies suggest that ocular symptoms are common in severe pneumonia. There are also occasional reports of conjunctivitis as the first symptom of SARS-CoV-2.^[9] However, there are no other reports except these two, and both are from China reporting varied frequency of ocular presentations. Hence, more research and evidence are required even from other parts of the world, for a comprehensive view on the ocular manifestations of SARS-CoV-2 and the associated risk factors.

Evidence is again limited to the presence of SARS-CoV-2 in tears. Xia J *et al.* evaluated CoV in tears and conjunctival secretions of patients with SARS-CoV-2 infections in 30 patients (21 common types and 9 severe types).^[10] Samples were collected at an interval of 2-3 days from tears and conjunctiva and only one patient with conjunctivitis yielded positive results in both tears and conjunctival samples. No virus particle was detected in tears and conjunctiva secretions in patients without conjunctivitis.^[10] Similarly, in another study, Agarwal R *et al.* collected 64 tear samples from 17 patients at different time points between days 3 and 20 after initial symptoms.^[11] No evidence of SARS-CoV-2 could be found in the tear samples, though one case had ocular symptoms, suggesting transmission through tears might be less likely.^[11] However, both the studies had limitations in terms of small sample size. The limited samples collected might be insufficient for real-time reverse transcription-polymerase chain reaction (rRT-PCR) tests for the detection of the virus. Most patients had also received antiviral treatment before sampling. Hence, the effect of the treatment cannot be excluded. Finally, no blood samples were analyzed to look at the association between serum viral load and viral shedding in tears. Xia J *et al.* also collected samples only once, which can also decrease the prevalence owing to false-negative results.^[8] Similarly, Agarwal R *et al.* collected only tears sample and no conjunctival sample was collected. More comprehensive research with a larger sample size is necessary to evaluate the role and definitive mechanism of SARS-CoV-2 in the eye. As SARS-CoV-2 has known to infect via ACE2 receptors, future studies should also verify the presence of ACE2 on corneal and conjunctival cells. Further studies are also needed to look at the association between serum viral load and viral shedding in tears. Finally, it is not clear how SARS-CoV ends in tears. It can be directly through the conjunctiva, or through the nasolacrimal duct or hematogenous infection of the lacrimal gland and the final mechanism needs better understanding.

However, the absence of virus in tears and conjunctiva does not eliminate the risk of transmission. If the ophthalmologist comes in contact with patients at close range during the

examination, the saliva of an infected person can still cause infection through conjunctival tissue. Another possible route suspected is aerosol. With aerosol-generating procedures, the virus may be concentrated in the air for a longer time.^[12] Route of transmission via ultrasound biomicroscopy, corneal confocal microscopy, etc., is still not proven, but theoretically, it cannot be ruled out.

There are reports of several ophthalmologists getting infected and also of mortality among ophthalmologists, despite being fully gowned with a protective suit and N95 respirator.^[9] It is crucial for the ophthalmologists to understand the ocular manifestations, as ophthalmology is a specialty where there is close contact with the patients. Understanding the ocular manifestation would not only aid in identifying early cases but also help in protecting oneself. However, until the exact mechanism is clearly understood, ophthalmologists and other healthcare workers should be more conscious to prevent transmission. It is essential to obtain each patient's travel history, any flu-like symptoms, as well as family history. Until further evidence is available, it would be prudent to regularly wash hands with soap and water and avoid touching eyes, nose, and mouth especially at-risk locations. In Hong Kong, ophthalmologists were recommended full Personal Protective Equipment (PPE) irrespective of patient status. Apart from this, equipment like B Scan probe, contact lens for photocoagulation, etc., should be strictly sterilized. Finally, ophthalmologists should do minimal routine ophthalmic procedures that are not urgent, as the risk of viral transmission may outweigh the surgical benefits.

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Conflicts of interest

There are no conflicts of interest.

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