COVID-19 pandemic from an ophthalmology point of view

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Coronavirus disease 2019 (COVID-19) is caused by a highly contagious RNA virus termed as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Ophthalmologists are at high-risk due to their proximity and short working distance at the time of slit-lamp examination. Eye care professionals can be caught unaware because conjunctivitis may be one of the first signs of COVID-19 at presentation, even precluding the emergence of additional symptoms such as dry cough and anosmia. Breath and eye shields as well as N95 masks, should be worn while examining patients with fever, breathlessness, or any history of international travel or travel from any hotspot besides maintaining hand hygiene. All elective surgeries need to be deferred. Adults or children with sudden-onset painful or painless visual loss, or sudden-onset squint, or sudden-onset floaters or severe lid oedema need a referral for urgent care. Patients should be told to discontinue contact lens wear if they have any symptoms of COVID-19. Cornea retrieval should be avoided in confirmed cases and suspects, and long-term preservation medium for storage of corneas should be encouraged. Retinal screening is unnecessary for coronavirus patients taking chloroquine or hydroxychloroquine as the probability of toxic damage to the retina is less due to short-duration of drug therapy. Tele-ophthalmology and artificial intelligence should be preferred for increasing doctor-patient interaction.

Key words Chloroquine - contact lens - coronavirus - eye donation - eye shields - hydroxychloroquine - ophthalmologist

Introduction

On December 31, 2019, the Government of China sounded the World Health Organization of a group of patients being admitted to hospitals with atypical pneumonia with likely origin due to a virus from the Huanan seafood marketplace in Wuhan city, situated in the province of Hubei in China¹. Initially, the virus was thought to have an animal-to-human transmission, but the enormous spread among humans due to the massive human migration on account of the Chinese New Year proved this fact untrue with the evidence of human-to-human transmission²⁴. Coronavirus disease 2019 (COVID-19) is a new infection that can affect both the upper and lower respiratory tracts through aerosols, faeces and contaminated surfaces⁵-⁸. However, no transmission through breast milk has been documented⁹. A potentially fatal form of it is known as severe acute respiratory syndrome (SARS)¹⁰. It is produced by a highly contagious RNA virus termed as SARS coronavirus 2 (SARS-CoV-2), with the tremendous capability of survival attributed to its rapid mutation rates as compared to DNA viruses¹¹. As of May 20, 2020, SARS-CoV-2 had affected 5,054,252 people in 213 countries/territories and two international conveyances, with 327,938 mortalities located majorly within the USA, Russia, Spain, Brazil, the UK and Italy¹². India had 112,028 people affected
with 3,434 total deaths, with the maximum being in the State of Maharashtra\textsuperscript{13}. This review highlights the risk ophthalmologists have due to close proximity with patients and suggests ways to prevent this transmission.

**Medical personnel at high-risk**

Ophthalmologists are at a high-risk due to the following three important reasons: presence of virus in the tear fluid, proximity of encounter and deceiving symptoms.

**Presence of virus in the tear fluid**

SARS-CoV-2 via its surface spike glycoprotein binds to the angiotensin-converting enzyme 2 (ACE2) receptors. These ACE2 receptors are found distributed in various human organs, including the surface of the cornea and the conjunctiva, and these act as potential entry points\textsuperscript{14,15}. Coronavirus was spotted in the conjunctival discharge of COVID-19-positive patients having conjunctivitis\textsuperscript{16}. Loon \textit{et al}\textsuperscript{17} have isolated virus from the tears of coronavirus-infected patients by reverse transcription-polymerase chain reaction (RT-PCR). While examining the patient, the risk of tears contaminating the fingers of the examiner as well as the instruments, is fairly high\textsuperscript{18}.

**Proximity of encounter**

Because of the proximity (20-30 cm) to the patients, examining a patient in the clinic (conjunctival discharge, tears and nasal/oral secretions) can pose a hazard to ophthalmologists\textsuperscript{19-21}. The patients visiting ophthalmology clinics are predominantly elderly and they suffer from old age-related diseases such as cataracts, macular degenerations and glaucoma\textsuperscript{22}. Hence, nosocomial infections are an essential concern both for the doctor and the patient\textsuperscript{23}.

**Deceiving symptoms**

Eye care professionals can also be caught unaware because conjunctivitis may be one of the first signs of COVID-19 at presentation, even precluding the emergence of additional symptoms such as dry cough and anosmia\textsuperscript{24}. The American Academy of Ophthalmology (AAO) has released an advisory alerting eye specialists to put on face and eye shields while examining patients with fever, breathlessness or any history of international travel or travel to and from any hotspot\textsuperscript{25}. With these reasons in the background, it is especially important to have practical and useful guidelines, directed at eye care specialists, tailored to the local needs to curtail the incidence of coronavirus infection in both medical personnel and patients.

**Guidelines for ophthalmologists to prevent the spread of COVID-19**

**Ocular involvement in patients with proven SARS-CoV-2 infection**

The symptoms of COVID-19 may vary from being completely asymptomatic to having fever, cough, breathlessness, muscle aches, fatigue and loss of smell or taste\textsuperscript{26}. Non-specific symptoms include headache, blood in vomitus or diarrhoea\textsuperscript{27}. A few COVID-19 patients present with conjunctival redness or conjunctivitis\textsuperscript{21}.

In a series of 38 patients from Hubei province in China, those with ophthalmic symptoms were more susceptible to have leucocytosis with increased neutrophil numbers and much higher enzymes such as procalcitonin, C-reactive protein and lactate dehydrogenase than patients with no ophthalmic manifestations. Ocular features were seen in one-third of the involved patients and they demonstrated signs of conjunctivitis, including conjunctival hyperaemia, chemois or increased tearing. Fundus was not evaluated in any of these patients. However, none of them complained of any decrease in vision. Nearly 91.7 per cent of the patients of the one-third in this study tested positive for SARS-CoV-2 using RT-PCR from nasopharyngeal swabs and of these, 16.7 per cent tested positive from both conjunctival and nasopharyngeal swabs\textsuperscript{28}.

In another study by Guan \textit{et al}\textsuperscript{26}, among 1,099 patients from mainland China, 0.8 per cent (9 patients) had symptoms of conjunctival congestion. In a case report of a 30 yr old patient of confirmed COVID-19, bilateral follicular conjunctivitis with tearing, redness and moderate and tender preauricular lymphadenopathy was documented on the day 14 of illness with the subsequent resolution on day 19. The fundus picture taken through a non-mydriatic fundus camera as well as macular optical coherence tomography was unremarkable. The virus load in the swabs obtained from the conjunctiva was considerably lesser than that obtained from the nasopharyngeal swabs\textsuperscript{29}.

**Ocular symptoms/signs as first indicators of SARS-CoV-2 infection**

In a prospective contact tracing study in China, the first symptom of a 22 yr old index patient of COVID-19 was itchy eyes\textsuperscript{30}. In another study which included
534 COVID-19-confirmed patients, 25 patients (4.68%) had conjunctival congestion and of them, three patients had it as the first symptom. The mean duration of the congestion was 4.9±2.6 days. Dry eye (112, 20.97%), blurred vision (68, 12.73%) and foreign body sensation (63, 11.80%) were the most frequently occurring ophthalmic symptoms in these patients. Other symptoms included itching and photophobia. Approximately more than 60 per cent of patients had a history of hand-eye touch. Other studies also demonstrated conjunctival congestion in 4.76 per cent and 2.78 per cent of the total COVID-19 patients, respectively\(^{32,33}\). In a contrary study of 17 patients, tear samples were negative for SARS-CoV-2, even though nasopharyngeal swabs were positive. One of the 17 patients demonstrated eye signs even though SARS-CoV-2 could not be established in tears. This study concluded that viral spread through tears irrespective of the stage of infection is less\(^{34}\).

Other coronaviruses are responsible for causing a wide spectrum of ophthalmic signs and symptoms such as conjunctivitis, uveitis and posterior segment vision-impairing conditions such as retinitis and optic neuritis. However, uveitis and other posterior segment manifestations have not been documented\(^{35}\). An illustrated depiction of all eye-related symptoms is given in Figure 1.

**Guidelines at the place of practice**

Non-pharmacological interventions, hygiene practices and personal protective equipment (PPE) to limit the virus circulation along with postponement of non-emergency surgeries should be followed in both public and private ophthalmology clinics\(^{21}\). Some of the important points are discussed below:

Opting for tele-ophthalmology: Only e-mails, phone calls, messages and social media platforms should be used to communicate with the patients. Tele-ophthalmology services can be used for patient consults or for patients requiring urgent follow up\(^{36,37}\). The governments in different countries have recommended telemedicine in lieu of in-hospital visits. Lives can be saved by social distancing in pandemic areas\(^{38}\). Mode of communication can be audio, video or text.

There are mobile apps for visual acuity and perimetry\(^{39,40}\). Home monitoring of intraocular pressure using finger tension and of metamorphopsia using Amsler grid should be done\(^{41}\). Drug dosage modifications can be done during teleconsultation. Informed consent of the patient needs to be taken during tele-consults or video visits. Doctor-patient interaction can also be enhanced through the Internet with the assistance of artificial intelligence\(^{42,43}\).

Screening at entrance to hospital: For any patient visiting the eye hospital, at the entry point, a history of travel in the past 14 days from an area in the red zone should be enquired about\(^{44}\). Thermal scanning should be done at the main entrance. The patient and the attendants should be asked to wear a three-ply mask. If the patient has fever or any of the aforementioned symptoms, he/she should be taken to the dedicated COVID-19 hospital\(^{45-47}\).

Triaging: Initially, telephonic triaging can be practised, and only those patients who require emergent ophthalmic check-up should be called to the hospital. Triaging should be able to segregate the patients into the following three groups: (i) patients who can be seen in the main stream (patients without symptoms and a history of travel to hotspots); (ii) patients who have to be sent to COVID-19 managing hospital; and (iii) indeterminate group. The indeterminate group should be evaluated for the need for urgent eye care.

![Fig. 1. Ophthalmological signs and symptoms of coronavirus disease 2019. Chemosis, conjunctival congestion, follicles, tearing, itching, dry eye, blurred vision, photophobia and preauricular lymphadenopathy are major signs.](image-url)
consultation. If urgent, they would need to be examined in a separate isolation room with PPE.

Emergent conditions: Patients with sudden-onset of painful or painless vision loss, or sudden-onset squint, or sudden-onset floaters or severe lid oedema and children with the aforementioned conditions as well as those with unilateral white reflex should be attended to on an emergent basis. For patients presenting with conjunctivitis, allergic or toxic conjunctivitis should be ruled out. Circumcorneal congestion can point towards serious ocular conditions such as uveitis or corneal ulcers. The final treatment can be targeted towards the most common causes of conjunctivitis i.e., viral/bacterial, which consists of a topical fluoroquinolone and lubricants. Topical steroids should be avoided as it would require frequent follow up for intraocular pressure monitoring. The latest guidelines by the All India Ophthalmological Society have given subspecialty-wise classification of procedure on the basis of priority: emergency, urgent and routine procedures.

Management at outpatient department (OPD): Children <10 yr and elderly >65 yr should be discouraged from visiting the hospital unless they are patients themselves. The waiting areas should be decongested and intercoms or call notifications on phones can be used to call each patient for examination.

Special referral tests such as refraction perimetry, optical coherence tomography, fundus fluorescein angiography, corneal topography, specular microscopy, ultrasound and ultrasound biomicroscopy should be deferred until these are critical for making a diagnosis. Fundus evaluation, if required, can be done using non-mydriatic fundus cameras. Indirect ophthalmoscopy should be preferred in place of the slit lamp for examination as it has a larger working distance. Indirect ophthalmoscopy can also be used for evaluating the central fundus in case of non-availability of non-mydriatic fundus cameras.

Management at operation theatre (OT) level: All elective surgeries should be postponed. Surgeries under general anaesthesia should be avoided as extubation leads to aerosol generation. Since nasal secretions have been shown to contain SARS-CoV-2; procedures which act as nasal simulants such as nasal endoscopy should be avoided. Topical anaesthesia should be preferred over regional anaesthesia. Pre-operative testing for COVID-19 should be done for all patients. Full PPE (N95 mask, fog and scratch-resistant goggles/face-shield, disposable waterproof gown, preferably nitrile gloves, and impermeable shoe covers) should be worn by surgeons while operating on COVID-19-confirmed patients. Proper technique of donning and doffing of PPE and their disposal should be followed. Separate colour-coded bins/bags should be kept as per the Biomedical Waste Rules 2016 and amended by the Central Pollution Control Board.

Instrument sanitation should be done after seeing every patient. Sanitation of the floor, doorknobs and bed rails should be done using freshly prepared one per cent sodium hypochlorite preferably after every two hours. The air conditioning should have fresh air exchange and should be fitted with standard filters. Temperature and humidity should be maintained as per guidelines. Negative pressure is preferred in rooms requiring aerosolization procedures such as intubation/extubation, suction and nebulization. A summary of potential strategies in hygiene practices, personal protective equipment and non-pharmacological interventions is documented in Figure 2.

Special topics of interest in COVID-19 era

Contact lens (CL) practice

A contact lens specialist should keep away from touching his/her face and mucus membrane-covered areas such as nose, mouth and eyes. CLs should be adequately cleaned, and disposable CLs should not be used longer than what is recommended. Individuals should be told to discontinue CL wear if they have any symptoms of COVID-19.

Corneal donation guidelines

The Eye Bank Association of America (EBAA): The Eye Bank Association of America has laid down guidelines for eye donation. According to these, eye banks should avoid corneal donation from donors who in the last 28 days were positive for the novel coronavirus or those who came in contact with a positive case or a suspect or those who had an acute respiratory illness with fever >38°C with any one of the symptoms of COVID-19 or those who had acute respiratory distress syndrome/pneumonia/ground-glass opacities on computed tomography. Cornea from a donor who has tested negative for the disease and has been diagnosed with another aetiology which explains the symptoms or findings can be considered for transplant.

Global Alliance of Eye Bank Associations (GAEBA): Because there is no evidence till date that coronaviruses
can be transmitted by avascular tissue (cornea) transplantation even though it has been proved to be present in tears and conjunctival discharges of patients positive for the novel coronavirus, any efforts to procure tissue are precautionary, hence, the guidelines include that any potential donor with confirmed or suspected coronavirus infection should not donate if the death has occurred less than 14 days since the resolution of symptoms or awaiting test results for suspected coronavirus infection. Moreover, if the donor has been in contact with a confirmed or suspected case of coronavirus infection less than 14 days from the first day of contact, the donation should be avoided.

Guidelines for cornea and eye banking should be followed.

Retinal screening before starting chloroquine therapy

Chloroquine (CQ) and hydroxychloroquine (HCQ) have been demonstrated to have considerable efficacy against the SARS-CoV-2. CQ and HCQ have been used by the physicians since long for diseases such as systemic lupus erythematous (SLE) as well as rheumatic disorders. Retinal toxicity is rarely seen before 10 or more years of use at a dose of <5 mg/kg real weight as advocated by the AAO guidelines. Rheumatologists have been routinely using HCQ as a part of the therapeutic regimen for SLE, myeloma and small-cell carcinoma of the lung. These regimens extend from a few weeks to months. Visual loss has not been documented in any of the studies except in two patients who showed subtle alterations in the parafoveal ellipsoid zone on optical coherence tomography.

Marmor has concluded that ophthalmic retinal screening is unnecessary for coronavirus patients taking CQ or HCQ as antiviral drug therapy for a time period less than two weeks, as the probability of toxic damage to the retina is extremely less even on
using large dosages. Other drugs such as remdesivir, CQ, oseltamivir, interferon 1β, tocilizumab and convalescent serum, as well as anti-mRNA vaccines, are under trial[7].

Conclusion

SARS-CoV-2 infection has evolved as a global health emergency in the present era. The risk of infection to the healthcare workers is very real, however, all healthcare professionals do not have the same risk. An ophthalmologist treating a presumably non-COVID-19 patient, especially with good triaging and exclusion of most of the potentially COVID-19-positive patients, is not exposed the same level of risk. Hence, ophthalmologists should work in tandem with infectious disease specialists for risk stratification and infection control measures as well as for the use of PPE. Till the time a cure is developed, artificial intelligence-based platforms, as well as tele-ophthalmology, should be encouraged.

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