

REVIEW ARTICLE



Coronavirus disease in ophthalmology practice: Current scenario; available evidence; and its implications

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Severe acute respiratory syndrome coronavirus 2 causes a highly contagious coronavirus disease named COVID-19 by the World Health Organization (WHO). It has emerged as a pandemic; number of affected individuals is only increasing and so is the spectrum of its clinical presentations. To control morbidity and mortality caused by COVID-19, all physicians including ophthalmologists, need to know its established as well as probable clinical presentations. Conjunctivitis can be the first presenting symptom of the disease. Ophthalmologists are at higher risk of contracting this infection due to close contact with the patient during different examinations and procedures. Examining such otherwise asymptomatic patients further increases the risk of infection. The present review updates about the current literature on COVID 19 in relation to ophthalmology. We need to control its spread at all levels, among patients and ophthalmologists, among staff as well as the community. Frequent disinfection and social distancing should be the new norm in clinics. Teleconsultation services need to be boosted and strengthened for future use along with efforts to end the pandemic.

Across the world, we are dealing with an unprecedented crisis and we are fraught with uncertainty. On December 31, 2019, the first case of pneumonia of an undetermined cause was reported from Wuhan in China. Since then similar cases flooded across the world and the disease was declared as Public Health Emergency internationally on January 30, 2020.^[1,2] On February 11, 2020, the World Health Organization (WHO) gave name to this coronavirus disease-2019 (COVID-19): COVID-19, and called the causative virus as “severe acute respiratory syndrome coronavirus 2 (SARS-COV-2).”^[1] Globally, as on, June 4, 2020, there are 6,416,828 confirmed cases of COVID-19, including 382,867 deaths, reported to the WHO.^[3]

SARS-COV-2 has far higher infectivity and low mortality than previously known human corona virus.^[4] It shows a rapid transmission during the incubation-period and may have milder symptoms in adults.^[5] Human-to-human transmission is commonly by fomites, droplets, aerosol, etc., similar to SARS virus. Risk of environmental contamination is also there, more by patients with the upper respiratory tract involvement. It has been shown that current decontamination measures are sufficient and hence there is a need for strict adherence to environmental and hand hygiene.^[6]

Clinical Presentation of COVID-19

COVID-19 can have a variable presentation. Fever and cough have been reported as the most common symptoms.^[7] In a study of 1099 Covid-19 confirmed patients^[7] from China, fever was seen at presentation in 43.8% of the confirmed COVID 19 patients and developed after hospitalization in 88.7%. The study also reported a difference in pathogenicity of the virus from SARS-CoV, and other seasonal influenza like illness, in view of absence of gastrointestinal symptoms. Other common symptoms include cough (67.8%), fatigue (38.1%), sputum production (33.7%), shortness of breath (18.7%), myalgia or arthralgia (14.9%), conjunctival congestion (0.8%), nasal congestion (4.8%), headache (13.6%), sore throat (13.9%), hemoptysis (0.9%), nausea or vomiting (5.0%), diarrhea (3.8%), and chills (11.5%). Signs reported to be seen frequently were: Tonsil swelling (2.1%), throat congestion 19 (1.7%), enlargement of lymph nodes (0.2%), as well as rash (0.2%).^[7] Children were earlier thought to be immune to the disease; but children affected by SARS-V-2 may develop a disease similar to Kawasaki’s illness as reported in another study.^[8]

SARS-COV-2 in Ophthalmology

The first alarm of COVID-19 was raised by an ophthalmologist only. The ophthalmologist Dr Li Wenliang identified seven cases with severe acute respiratory symptoms but was accused of raising a false panic. He later acquired the virus from an asymptomatic glaucoma patient and expired.^[9]

Possibility of transmission through ocular route is there due to the presence of similar angiotensin converting enzyme 2 (ACE2) receptors on ocular as well as host surfaces.^[10] The mechanism behind transmission is the same as SARS,^[11] i.e., through exposed mucous membrane. The other routes include transmission through the nasolacrimal duct, from where virus migrates to inferior meatus. Transmission can also occur from the ocular mucosal immune system related with lymphoid tissue in the nasolacrimal duct as well as nasal cavity.^[10]

Ocular involvement is reported in COVID19 patients up to the extent of 31.6% and more common in patient with severe disease.^[7,12] Ocular involvement was reported as the presenting symptom in some studies and in others reported around 2 weeks of onset of illness.^[12-15] In otherwise healthy individuals; conjunctivitis may also be reportedly the first presenting symptom.^[13,14] Many reported cases manifested ocular symptoms coherent with conjunctivitis, i.e., conjunctival congestion, conjunctival chemosis, increased tearing, preauricular lymphadenopathy, or acute follicular conjunctivitis. Tears and conjunctival secretions are infective in most cases with conjunctivitis. In multiple studies, conjunctival swabs and tear of patients with conjunctivitis showed reverse transcription polymerase chain reaction positive for SARS-COV-2, and negative for those without conjunctivitis. However, the detection of the virus was lower from conjunctival swabs than from respiratory samples.^[12,14-17] Even viral conjunctivitis can also be the presenting sign in many cases.^[13,14,18] Hence, conjunctiva can act as a possible source as well as route of transmission.^[19,20] Other routes includes hematogenous spread to lacrimal gland or migration through the nasolacrimal duct.^[21]

Patient can also present with acute hemorrhagic conjunctivitis with pseudomembranous as reported in one study.^[16] The first ocular manifestations reported in the case was conjunctival hyperemia and clear secretions, on day 17 suggesting a viral conjunctivitis. Bacterial or viral etiology was excluded on conjunctival scrapings and swabs. The treatment prescribed for the conjunctivitis was eyelid hygiene, eyewash with physiologic serum and artificial tears. Two days later, clinical signs were exacerbated with follicles, petechiae, tarsal hemorrhages, and chemosis with thin yellowish-white translucent membranes on the tarsal conjunctiva of lower lids. The membrane was identified as pseudomembranous as it could be easily peeled off without bleeding. Superficial punctate keratitis, mucous filaments, and tarsal pseudo membranes were seen on fluorescein and blue light examination. There was no intraocular involvement. By day 20, tear samples and conjunctival secretions were negative for SARS-CoV-2. Treated with eye drop azithromycin BD for 3 days, along low dose topical dexamethasone and to avoid conjunctival

fibrosis and retraction routine removal of pseudo membranes was done. Symptoms improved, without any complications.^[16]

Iatrogenic orbital complication can also occur with COVID-19. A case of orbital emphysema was reported in a 74-year-old man with COVID-19 associated pneumonia, who required orotracheal intubation in view of respiratory failure.^[22] Prone positioning and high positive end-expiratory pressure ventilation were provided in view of refractory hypoxia. On supination, patient had subcutaneous emphysema from the chest to the face, extending to bilateral eyelids, and unilateral conjunctiva. There was no sign of vascular occlusion or orbital compartment syndrome.

Intraocular involvement in COVID 19 cannot be excluded. This is because ACE-2 is a cellular receptor for SARS- CoV-2 and the same receptor also found on conjunctival and choroid epithelia, and vascularized retinal pigment epithelium.^[23-25] Animal experimental studies have shown ocular manifestations such as conjunctivitis, pyogranulomatous anterior uveitis, and retinal vasculitis choroiditis with retinal detachment.^[26] Retinal optical coherence tomography (OCT) changes in 12 COVID-19 patients included hyper-reflective lesions at ganglion cell and inner plexiform layers levels markedly at the papillomacular bundles. OCT-angiography and ganglion cells analysis was reported to be normal. Four patients had microhemorrhages and subtle cotton wool spots around retinal arcade, otherwise no evidence of intraocular inflammation was noted.^[27] Hence, we may come across retinitis and optic neuritis associated with SARS-COV-2 in future. Patients with ocular involvement were probable to have higher white blood cell counts and neutrophils, C-reactive protein, procalcitonin, and lactate dehydrogenase in a study.^[12]

What an Ophthalmologist Should Know?

Like the whole world, medical fraternity being frontliners to SARS-COV-2; adapted immediately. Outpatient departments (OPDs) were closed, emergency services continued. Tele-consultation was started with all possible means throughout world. Despite limited personal protective equipment (PPE) supply, health worker served and paid highest price in this battle. Over 90,000 health workers are infected with COVID-19, all over the world.

Not only does the COVID19 cause physical morbidity but also has a psychological impact on ophthalmologists. An online survey on mental health of ophthalmologists and ophthalmology trainees during lockdown was conducted by the All India Ophthalmological Society and Indian Journal of Ophthalmology where 32.6% ophthalmologist reported some form of depression.^[28]

Literature says that health workers in non-COVID area (including ophthalmology) are affected more than those in COVID areas. A large proportion of ophthalmologists have switched over to telephonic advice or other forms of telemedicine to assist patients.^[29] Here are some pointers to help ophthalmologists in this time of the pandemic.

Management of COVID-19

General management

According to the WHO; at present no effective medications or vaccines available for the prevention or treatment of the SARS-CoV-2.^[30] China International Exchange and Promotive Association for Medical and Health Care (CPAM) recommends use of lopinavir; ritonavir (2 capsule BD) along with nebulized alpha-interferon (5 million units in Sterile Water for Injection inhaled twice daily).^[31,32] A group of Korean physicians recommended not to use antiviral medications for young, healthy patients with mild symptoms and no underlying comorbid conditions. They recommended treatment with antivirals such as lopinavir 400 mg; ritonavir 100 mg (2 tablets oral BD) or chloroquine (500 mg BD Oral) to elder patients or patients with comorbid conditions. They recommended use of hydroxychloroquine (400 mg BD Oral) in case of unavailability of chloroquine. In view of side effects, use of ribavirin and interferon was recommended only if treatment with ritonavir, lopinavir, chloroquine, and hydroxychloroquine was unsuccessful. With the onset of pandemic hydroxychloroquine was recommended by multiple studies for treating and for prophylaxis of COVID-19 patients.^[33-36] Contrary to early small studies, recent larger studies do not support hydroxychloroquine for in-patients who required oxygen.^[37] Screening for long QT syndromes, concomitant QTc prolonging medicines, or glucose-6-phosphate dehydrogenase deficiency should be mandatory before prescribing prophylactic hydroxychloroquine. This it is a difficult task. In addition, complications secondary to untested drug with benefits still unknown will only increase burden on already overwhelmed health-care system. Safety profile of immunomodulators in population at risk of severe viral disease is under studied.^[38] Remdesivir (GS-5734), a nucleoside analogue and sofosbuvir in combination with ribavirin, is seen as potential future treatment options.^[39] Apart from drugs general treatment recommendations include bed rest, supporting treatment, and monitoring vital signs; routine laboratory tests for blood and urine, C-reactive protein, serum biochemical indexes, and coagulation function; antiviral therapies with atomized inhalation of α -interferon and lopinavir or ritonavir in suitable patients; and oxygen support should be given to patients with a low blood oxygen saturation and long-term use of corticosteroids for treating viral pneumonia or acute respiratory distress syndrome to be avoided. Respiratory support is reserved for patients in severe or critical conditions in the form of non-invasive or invasive ventilation as per requirement. Prone position ventilation: Lung recruitment maneuver or extracorporeal membrane oxygenation are other options that can be used.

Management of ocular involvement in COVID-19

As most of studies showed conjunctivitis as most common presentation; treatment of COVID-19 related conjunctivitis is like that of adenoviral conjunctivitis depending on presentation.

Strict ocular and hand hygiene are recommended as virus is known to be present in tears and ocular secretion of COVID-19 patients with conjunctivitis.^[12-15] Tailored treatment according to the presentation is needed. For acute follicular conjunctivitis, lubricants with cold fomentation are enough. Prophylactic topical antibiotics can be added. A combination of an antibiotic and a lubricant, for example, ciprofloxacin hydrochloride 0.3% or moxifloxacin hydrochloride 0.5%, and carboxymethyl cellulose 0.5% or sodium hyaluronate 0.1%, 4–6 times a day for 2 weeks, can be a standard pre-prepared package that can be dispensed immediately to the patient and can avoid prolonged stay of patient in clinic or hospital premises.^[40] Ribavirin eye drops can be prescribed 4 times/day.^[17] Acute hemorrhagic conjunctivitis with pseudo membranes, needs to be treated with topical antibiotics, low doses of topical dexamethasone with routine debridement of pseudomembranous to avoid complications such as conjunctival fibrosis and retraction.^[16] For analgesia, oral paracetamol should be preferred over nonsteroidal anti-inflammatory drugs like ibuprofen as they have been shown to worsen the systemic effects of COVID infection.^[41] It is best to avoid topical oral steroids as frequent follow-up for IOP monitoring does not seem rational and doable in a pandemic. Follow-up should be scheduled at 2 weeks with home quarantine, signs of worsening should be explained, which should be encouraged to get teleconsultation within a week or whenever needed before that. In case of worsening of ocular symptoms along with the presence of symptoms consistent with COVID-19 as mentioned earlier, low dose steroid can be added with antibiotics and should be referred to physician or COVID-19 referral center. If no COVID-19 symptoms are present, patient can be sent home and to be followed up after 2 weeks or by teleconsultation.^[40] Involvement of anterior segment, posterior segment, or optic neuritis is described sparsely till now, but possibility cannot be excluded. Hence, a detailed anterior segment and fundus examination should be done.

Prevention of Spread of COVID-19

Among public and patients

Until we control this pandemic with an effective therapy or vaccine, clinics need to decrease overall footsteps and to mandate social distancing. All nonurgent appointments and surgeries should be postponed. This is right time to strengthen and streamline teleconsultation department in all hospitals and private practices using different modern methods of communication. A system should be developed for taking prior appointments, and for proper spacing between two consultations. There should be single point of entry to hospital where patients, attendants, and all staff should be screened with simple questionnaires to assess risk of prior exposure and thermal scan. Consent must be taken for undergoing treatment or work in the setting of exposure risk to COVID 2. Social distancing to be followed strictly in waiting areas, proper ventilation of area

with exhaust fans and opening maximum no of doors, separate door for entry and exit if possible with hand sanitizer at door. Pediatric and geriatric, immunocompromised patients should be seen on priority. Limited use of lifts, avoiding unnecessary touch to doorknobs, walls, staircase railings, hospital furniture to be stressed. Educative material should be displayed on sign boards, or through simple animations on screens.

All should wear masks depending on the risk of exposure. One separate room should be designated for the care COVID-19 cases, suspects, and exposed patients. Staff in this isolation room should be equipped with adequate PPE. All health personnel should ensure frequent hand washing. All known or suspected cases should be reported to authorities so that proper measure can be taken at level of community and administration.^[42]

Disinfection

Waiting and emergency rooms areas should be sanitized after every 2 h or after every 3 patients. The emergency room areas doorknobs, silt-lamps (head and chin rest), etc., must be cleaned with freshly prepared 1% Sodium Hypochlorite or 1% Bacillocid Extra solution. Floor and common contact surfaces must be cleaned with 1% Bacillocid Extra solution before work begins and every 2 h with Lizol. Equipment such as ultrasound biomicroscopy probe, USG probe, specular microscope, lenses, indirect and direct ophthalmoscopes, pen, and torches, and other such items should be disinfected and cleaned frequently. Patient and doctor should not speak during a close examination.^[42]

From patient to ophthalmologist and other staff

Ophthalmic professionals are advised to take three-level protective measures.^[43] A study from Hong Kong laid some basic guidelines for all ophthalmologists.^[44] All healthcare workers (HCW) coming in direct patient contact should change into surgical scrub suits at the entry to the hospital and change out to street clothes at the exit and to take a soap bath at once they reach home. History taking regarding COVID-19 symptoms or exposure is mandatory.^[45] All staff should be encouraged to bring minimum possible personal items to the hospital. Equipment like 90D lenses, indirect ophthalmoscope should be kept in clinic. Different methods of examination such as direct ophthalmoscopy, Goldman applanation tonometry, and slit lamp examination require close contact to patients and increase risk of transmission from patient to ophthalmologist. Hence, all protective measures should be taken examining every single patient as even asymptomatic patients with COVID-19 or patients in incubation can transmit the disease.^[5] Alternative equipment can be utilized such as handheld portable Tono-Pen as an alternative to conventional Goldmann applanation tonometer for measuring intraocular pressure and fundus photography or binocular indirect ophthalmoscope instead of fundus examination. Handmade or commercially available protective breath shields must be installed on slit lamps and wearing masks is mandatory. There are reports on transmission by aerosol contact with conjunctiva if no eye protection is worn.

In clinics mask to be worn carefully to cover mouth and nose. Mask should not be touched in between and should be removed properly with lace without touching in front. Three-ply surgical mask/N 95 masks to be used for not more than 8 h.^[42] Patient should also be wearing a mask and gloves, if possible.

Operating room precautions

All patients with conjunctivitis should be considered as COVID-19 suspect, to be seen in a designated OPD room with an isolated waiting room by a designated ophthalmologist in full PPE. Optimize support staff and HCW allocation (one-third to half of the regular staff per day. We should develop a dedicated COVID-19 operation room, better a negative pressure room with separate area for donning/doffing of PPE. Seniors should do surgery choosing quickest procedure available. Dedicated COVID-19 anesthesia team should be there. Testing should be performed before operating on an asymptomatic suspected COVID-19 patient. A physician fitness to be obtained for every patient including ruling out airway pathologies, particularly underlying pneumonia. Unnecessary staff should be avoided in the operating room. Surgeon and other staff should wait outside at time of intubation and extubation. Time between two subsequent surgeries should be increased. Patient should wear mask on the way to operating table. PPE should be worn properly. Since SARS-CoV-2 particles have been found in nasal swabs, pharyngeal swabs, sputum, tears, and blood; therefore, procedures such as dacryocystorhinostomy; both external and endoscopic are now classified as “high-risk” procedures.^[46] For other oculoplastics procedures; avoiding general anesthesia, cautery; repeated irrigation and suction; and avoiding endonasal approach are recommended. Risk stratification is needed in all ophthalmic subspecialties.

Sanitizer aerosol driven ocular surface disease is another drawback of our vigorous hand hygiene practices.^[47] More studies are required to know the whole spectrum of ocular involvement in COVID-19. Knowing whole profile of ophthalmic manifestation of COVID-19 will allow us to diagnose early and to provide better and appropriate treatment.

Among hospital staff

For safety and to ensure the availability of manpower when needed, it is important to have a duty roster so that only one-third to one-half staff is working at any given time. The residents and fellows must be also given specific duties so that all of them do not enter the hospital and crowd the emergency/OPD areas. Only necessary staff, optometrists, and nurses must be called. If any HCW, has any travel history to international/national conferences in areas that bring high risk, or has developed symptoms, or has a family member with symptoms, should be strictly quarantined, and the nearest authorities should be informed. Teaching activities can only be performed using online portals such as web meetings and other mobile apps. Staff should minimize socializing in break times.^[42]

Environmental spread

We do not have complete knowledge about alternate routes of transmission, namely, through sewage, contaminated water, or air conditioning systems. Hospital waste should be disposed responsibly according to biomedical waste guidelines. As virus shedding in stool and other secretion reported so toilets, bathrooms to be cleaned frequently with proper disinfectant.^[6]

Effective mitigation strategies

The COVID-19 infection has led to an unprecedented number of infections and deaths in recent times and continues exposed loopholes in our present health-care system. Like studies from earlier respiratory viruses guided us in treatment and prevention strategies, our efforts to strengthen our health-care system and experience with SARS-COV-2 will guide us in future. COVID-19 should be taken as opportunity to build resistance and resilience against such epidemic or pandemic in future. We need to enhance our health-care system with a greater number of health workers, ventilators, PPEs, and other essential equipment. We need to include training such as donning/doffing PPEs, wearing masks with proper technique, and of proper size in our routine training programs. A whole quality check system for quality control of PPEs needs to be established. We need to robust triage system in hospitals by training and building suitable infrastructure. Teleconsultation empowered with modern technologies has emerged as a rescue system to conventional health-care system in this pandemic time. We need to put more efforts to exploit all the possibilities that teleconsultation can serve. Meanwhile, we should support and lead governments campaign for awareness related to COVID-19 and social distancing.

The pandemic of COVID 19 has affected ophthalmology more than we know and more than we can prove. Ophthalmologists can be the first physicians to evaluate a patient with COVID-19; as conjunctivitis is a common presenting condition.^[48] SARS-CoV-2 transmission through tears may be possible, even in patients without symptomatic ophthalmic involvement.^[49] The use of PPE covering the face, nose, mouth, and eyes should be mandatory even when examining a conjunctivitis patient as conjunctivitis caused by COVID 19 is clinically indistinguishable from other viral follicular conjunctivitis.^[50] The impact on teaching and resident learning has taken a setback which will be measured only in the times to come.^[51] We do have established guidelines for re-starting our ophthalmology as well as subspecialty practice to guide us during and even after the lockdown period.^[52] Teleconsultations, prebooked appointments, triage outside the eye clinics, home dilation, slit lamp and face shields, masks worn by the patient, as well as the treating doctor should be the new normal. Compared to social restrictions, prompt detection, isolation of cases, proper quarantine, and social distancing seems more effective in controlling outbreak. Social distancing also needs to be continued for several months to have a lasting impact. It has been predicted that by reducing the human-to-human contact by 90%, we can stop the epidemic. Hence, social distancing needs to

be practiced for several months to have lasting impact, we need to embrace social distancing as a part of our daily life.^[53-56] For an ophthalmologist, use of PPE such as masks, gloves and protective eye wear should be a routine while examining all patients and not just suspects.

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