

## Ocular Implications in COVID Era: A Challenge

Anuradha Raj<sup>1\*</sup> and Nikhil Agrawal<sup>2</sup>

<sup>1</sup>Associate Professor, Department of Ophthalmology, All India Institute of Medical Sciences, Bathinda, Punjab, India

<sup>2</sup>Assistant Professor, Department of Ophthalmology, All India Institute of Medical Sciences, Bathinda, Punjab, India

**\*Corresponding Author:** Anuradha Raj, Associate Professor, Department of Ophthalmology, All India Institute of Medical Sciences, Bathinda, Punjab, India.

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### Abstract

Coronavirus disease 2019 (COVID-19) is an ongoing pandemic, and this virus spreads mainly during close contact by tiny droplets. Ocular surfaces being a potential mode for the transmission, ophthalmologists are highly prone to acquire this infection. Due to the presence of angiotensin-converting enzyme 2 in various ocular tissues and cytokine storm lead to vasoconstriction, ischemia, hypercoagulopathy and thromboembolic phenomenon, this virus binds easily and shows various ocular manifestations such as conjunctivitis, retinal vascular occlusions, worsening of diabetic retinopathy, ocular nerve palsies and orbital mucormycosis. Proper ocular care and awareness among the medical fraternity need the hour for prompt diagnosis and management to avoid irreversible sight loss.

**Keywords:** Coronavirus Disease 2019; Central Retinal Artery Occlusion; Hyper-Coagulopathy Mucormycosis

### Abbreviations

COVID-19: Coronavirus Disease 2019; SARS-Cov-2: Severe Acute Respiratory Syndrome Coronavirus 2; ICU: Intensive Care Unit; ACE2: Angiotensin-Converting Enzyme 2; CPAP: Continuous Positive Airway Pressure; IOP: Intraocular Pressure; CRAO: Central Retinal Artery Occlusion; CRVO: Central Retinal Vein Occlusion; AAO: American Academy of Ophthalmology

### Introduction

Coronavirus disease 2019 (COVID-19) is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). This outbreak emerged in December 2019 in the seafood market Wuhan city, situated in China, presenting fever, cough, fatigue and diarrhoea [1,2]. This COVID-19 was declared a pandemic by the WHO on 11<sup>th</sup> March 2020 [3]. COVID-19 spreads through droplets of respiratory secretions, aerosols, faeces, contaminated surfaces and can affect both the upper and lower respiratory tracts [4]. This virus tends to recognize and bind angiotensin-converting enzyme 2 (ACE2) host receptor which is present in various tissues and cell types, including cornea and conjunctival epithelium [5,6] retina [7], vascularized retinal pigment epithelium and choroid [8].

The Chinese Ophthalmologist Li Wen liang died after contracting virus from a glaucoma patient, raising global concern among Ophthalmologists. Due to ACE 2 receptors in ocular tissues, tears, conjunctivitis as a feature, proximity examination and ocular surface as a gateway for virus entry, Ophthalmologists are more prone to contract the infection.

### Various ocular manifestations in different clinical scenarios

#### Cornea and ocular surface

Bilateral follicular conjunctivitis is the usual presentation of COVID-19 with chemosis, watery discharge, mild lid oedema and enlarged preauricular and submaxillary lymph nodes. Unilateral kerato-conjunctivitis can be its first manifestation [9]. Patients admitted to intensive care unit (ICU) can develop various ocular surface disorders and Infective keratitis due to the ICU environment enclosing drug-resistant bacteria, continuous positive airway pressure (CPAP), oxygen masks, sedation leading to by excessive dryness, conjunctival chemosis, lagophthalmos and eventually exposure keratitis [10]. Prone and positive pressure ventilation can lead to a subconjunctival haemorrhage [11]. Depending upon the viral load, conjunctivitis can be self-limiting or aggressive.

The conjunctival swab can be taken for reverse transcriptase-polymerase chain reaction (RT-PCR) and can be treated with Azithromycin eye drops twice daily along with mild steroids to cover the inflammation.

#### Neuro-ophthalmological complications

The neuro ophthalmological manifestations of COVID-19 can be diplopia, ophthalmoparesis or ophthalmoplegia involving the cranial nerves showing abnormal perineural MRI findings [12].

#### ICU implications

Prone positioning in COVID ICU help to increase lung expansion and perfusion, reducing ocular perfusion by increasing venous pressure and intraocular pressure (IOP) [13]. In addition, various comorbidities such as diabetes, hypertension, and atherosclerosis also lead to ocular hypoperfusion by increasing vascular resistance. Prone can precipitate acute angle-closure glaucoma. Dryness can be encountered due to positive pressure ventilation and the use of various types of oxygen masks. The discontinuation of prone is mandatory after a short while to avoid complications. Highly viscous lubricants, eye drops and ointments can be helpful to reduce dryness. In cases of lagophthalmos, tape tarsorrhaphy or surgical tarsorrhaphy can be done to avoid exposure keratitis that can otherwise aggravate endophthalmitis or pan-ophthalmitis in sepsis cases. Ocular complications can happen in ICU care and especially in cases of invasive mechanical ventilation and the health care staff should be aware of this fact.

#### Retinal implications

The cytokine storm leads to vasoconstriction, inflammation, ischemia, hypercoagulopathy and thromboembolic phenomenon leading to vascular occlusion such as central retinal artery occlusion (CRAO) [14]. The combined cavernous sinus thrombosis and CRAO can be one of the manifestations of COVID 19 without any co-morbidities in younger patients [15]. Even the occurrence of unexplained central retinal vein occlusion (CRVO) in the era of COVID-19 in young patients can be one of the presentations. In all these cases of the vascular occlusions, early detection and treatment can help restore vision that otherwise can be lost [16].

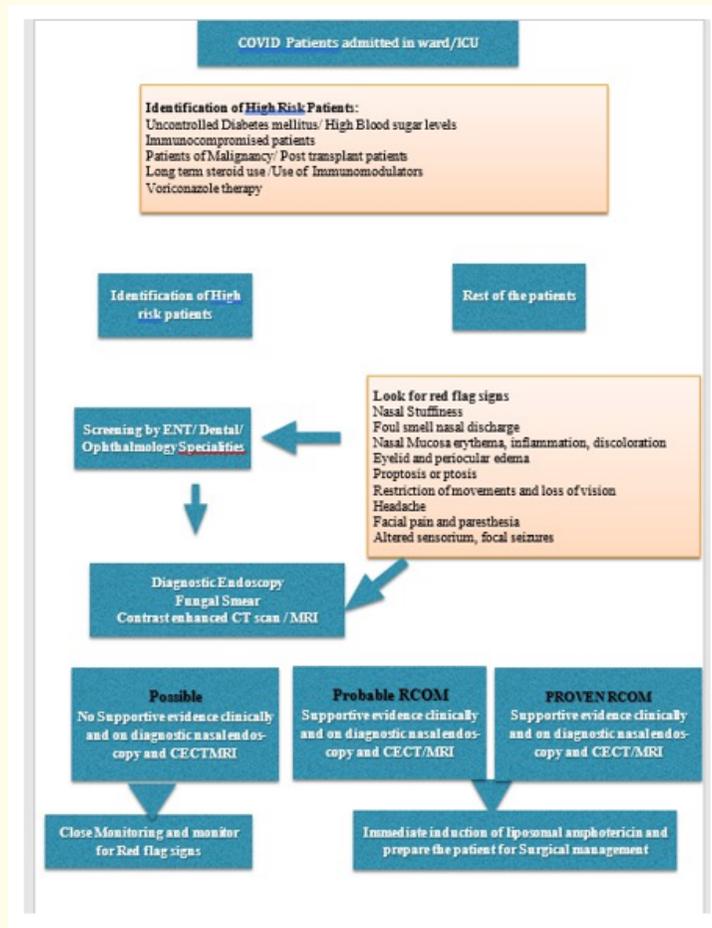
As COVID is associated with hyper-glycemia due to concurrent usage of intravenous steroids and stagnant lifestyle, these cases land up with the emergence of diabetic retinopathy changes or worsening of diabetic retinopathy. In addition, thrombotic microangiopathy in the form of cotton wool spots and micro-haemorrhages on fundus examination with normal pupillary reflexes can be seen. The management of diabetic retinopathy can be done after the patient gets COVID free unless it is sight-threatening.

The Ophthalmologist has to bear the responsibility to control the viral spread and ensure the health-care worker's safety by changing the routine clinical practice. In order to decrease infection of both the patients and the eye care providers, various practice protocols are established.

A three-level approach including protective measures and personal protective equipment (PPE), environmental and administrative control measures can help control the spread of COVID -19 infection [17]. In addition, telemedicine has also gained tremendous popularity for providing medical care to needy patients remotely [18].

**Out- patient department (OPD) protocols**

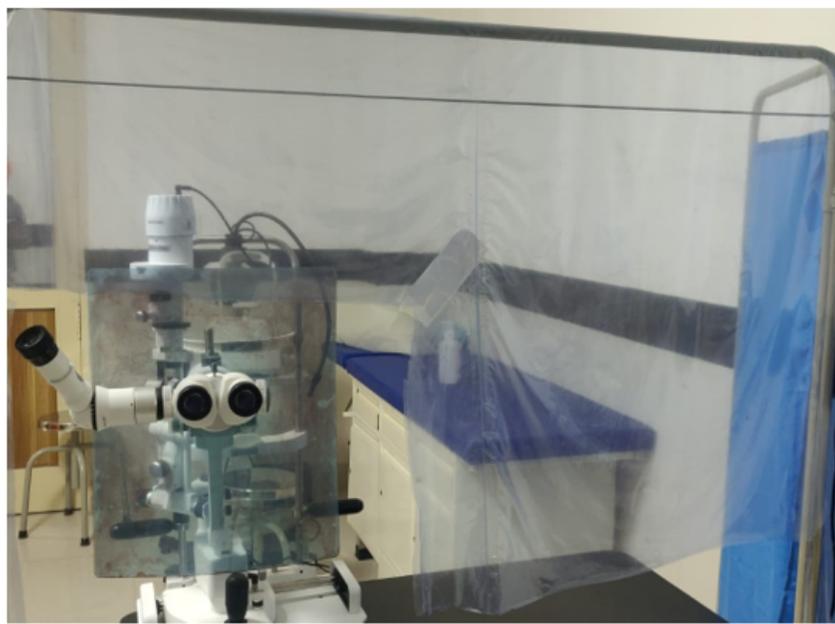
The first presenting symptom in a COVID-19 patient can be conjunctivitis, and it has the potential to spread by ocular surface, tears and conjunctival secretions, which harbour this virus. Sitting of patient should be organized by sparing one chair to allow social distancing (Figure 1). The strict use of eye protection in the form of goggles or face shields, gowns, gloves in addition to N95 masks or PPE kit while examining the COVID-19 suspect patient has been recommended by The American Academy of Ophthalmology (AAO) [19] COVID-19 infection transmission can occur while examining eye without eye protection [20]. Slit-lamp examination being nearby, the patient should be advised to speak less as it can lead to aerosol transmission. Imaging in case of chronic retinal diseases or glaucoma, the minimal contact time should be followed in these patients. In cases of suspects, a separate area can be allocated for the imaging [21,22]. The bedside or on-call Ophthalmic examination can be done by indirect ophthalmoscopy using PPE kits in COVID -19 infected patients.



**Figure 1:** Depicting the flow chart for rhino sinus orbital mucormycosis management.

### Trends of environmental control

Proper air ventilation in the waiting and examination area of OPD should be ensured by diluting the air. The large plastic protective screens installed on slit lamps act as a barrier between the Ophthalmologist, and the patient should be used to enhance the protection of both (Figure 2). AAO also recommended the use of such screens. Various equipment and instruments used in ophthalmology OPD such as slit lamps, protective shields, tonometer tips, keyboards, furniture surfaces should be disinfected after each patient's examination. Even the B-scan probe and laser lenses need disinfection and proper sterilisation protocols. The use of diluted household bleach can be used as COVID-19 specific disinfectant. The disinfectants of at least 70% alcohol and mixing five tablespoons of bleach per gallon of water were recommended [24].



**Figure 2:** Showing special arrangement installed on the slit lamp to reduce transfer of infection.

### Changes in administrative control

Proper triaging based on symptoms such as fever, sore throat, dry cough, headache, loss of taste/smell, diarrhoea, history of travel to endemic hot spots and contact of confirmed or suspected COVID-19 can be done before entering the OPD premises.

If a patient shows, any symptoms should be suggested for investigations for COVID-19 and referred to the same to the proper care centre. Ocular emergencies should be tackled, and all the elective procedures and non-urgent visits can be postponed. Social distancing should be aggressively followed in the waiting area by blocking the alternate seats. In-person, meetings should be deferred. All the lectures, academic and administrative meetings should be conducted online. If the patients in isolation require the Ophthalmologist, they should be arranged in the shifts and kept on call.

Li., *et al.* in 1999 described ophthalmic telemedicine centres setups for the first time [25]. The telemedicine platform is a boon for the management of chronic ophthalmic conditions by reducing the direct patient-doctor encounter [26]. On video consultation, the emergen-

cy patients can be grossly examined and called in or referred without delaying the management. Suspected or confirmed COVID 19 cases with non -urgent ophthalmic complaints should be referred for medical care. In confirmed cases of COVID-19, if urgent, these patients can be examined in isolated areas with all the precautionary measures.

### Management of ocular emergency

The emergencies in Ophthalmology include phacomorphic glaucoma, angle closure glaucoma, active keratitis, large corneal perforations, corneal graft rejection, chemical or thermal injuries, central retinal artery occlusion and orbital mucormycosis. Cataract surgery is warranted in cases of phacomorphic glaucoma. Angle closure glaucoma can be managed by using intravenous hyperosmotic and topical antiglaucoma medications. The cases with infective keratitis with perforation should be managed with therapeutic penetrating keratoplasty. Chemical burns and injuries should be managed with topical antibiotics, cycloplegics, antiglaucoma and lubricants eye drops and ointments after complete ocular irrigation.

### Mucormycosis

Mucormycosis, a subtype of zygomycosis, is an aggressive, opportunistic infection.

Given the ubiquitous nature of fungi, humans are exposed on a regular basis; however, it rarely causes an infection in one with an intact immune system. Mucormycosis predominantly affect the oral cavity, nasal and paranasal sinus, orbit and brain predominantly, but the fungi can also infect other body areas such as the gastrointestinal tract, skin, and other organ systems [27,28].

The sudden exponential increase in the cases of mucormycosis in patients of COVID is a matter of immediate concern. Rhino-cerebro orbital mucormycosis is a potentially lethal, angio-invasive fungal infection triggered by diabetes mellitus, mechanical ventilation, prolonged voriconazole therapy, immunodeficiency disorders, and corticosteroids immunosuppressive drugs use [29,30]. Therefore, early diagnosis supported by a high index of clinical suspicion and multidisciplinary approach comprising of experts in diagnosis (radiology, microbiology, pathology, molecular biology), medicine (infectious disease, neurology, critical care) and surgical (otorhinolaryngology, ophthalmology, neurosurgery) care is required to optimise outcome and minimise morbidity.

Clinical suspicion is supported by warning signs like nasal stuffiness and discharge, foul smell, epistaxis, eyelid, periocular and facial oedema, discolouration or pain, sudden loss of vision, proptosis, and restriction of ocular movements raise the alarm for treating physician. This should be followed by diagnostic nasal endoscopy, fungal smear, contrast-enhanced CT scan and contrast-enhanced MRI in case of orbital involvement.

Patients with high suspicion of mucormycosis supported by direct microscopy and radiological features should be administered total doses of liposomal amphotericin b 5 - 10 mg/kg or Posaconazole 300 mg iv twice a day [29] (Figure 3).



**Figure 3:** Demonstrating spacing of a chair in between to ensure social distancing.

In cases of predominant paranasal sinus involvement, early debridement of paranasal sinuses with turbinectomy, palatal resection should be done to achieve clear margins. Furthermore, retrobulbar injection of amphotericin and irrigation of paranasal sinuses with amphotericin could be done. In cases of orbital involvement, exenteration should be done. However, combining two anti-fungal is not recommended but step down oral antifungal therapy is warranted [31].

The incidence of mucormycosis could be reduced by judicious and supervised use of systemic corticosteroids and tocilizumab, proactive metabolic control, maintaining the aseptic condition while administering oxygen. Additionally, training of paramedical staff and awareness among the general public to identify red flag signs are an essential part of early diagnosis and management.

### Summary

The ocular implications of COVID-19 are on the rise with time. Therefore, it is essential to a safe environment by segregating the patients as suspected or probable or confirmed cases of COVID-19. Non-urgent and probable or confirmed COVID-19 cases can be guided and referred to for medical treatment. If there is ocular urgency or emergency, they must be evaluated in a designated isolated clinic. Strict protocols need to be imposed to reduce the chances of transmission of this infection by asymptomatic carriers to the Ophthalmologist and the health care staff.

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