

OCULAR MANIFESTATIONS OF COVID-19

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ABSTRACT

SARS-CoV-2 (severe acute respiratory syndrome-coronavirus-2) is a coronavirus that causes COVID-19 (coronavirus disease 2019) with mild to severe respiratory illness. It is a highly contagious disease transmitted via respiratory droplets and other routes still being investigated either through a direct or indirect contact with infected people or contaminated surfaces. It is well known that coronaviruses (CoVs) can cause a variety of ocular pathologies in animals, including conjunctivitis, anterior uveitis, retinitis, and optic neuritis, many of which are severe. However, there is no evidence to support the presence of the SARS-CoV-2 in the eye tissue of asymptomatic patients, even if the symptomatic incidence is low.

COVID-19 has spread throughout the continents and has become a global threat to public health as it posed the risk of rapidly overloading health care systems and causing grave mortality worldwide. As a result of this, the World Health Organization (WHO) on March 11, 2020 declared coronavirus a global pandemic.

While diagnostic and therapeutic efforts have been focused on respiratory complications of the disease, several studies have described a few cases with initial ocular symptoms followed by systemic symptoms of the disease. SARS-CoV-2 RNA has been found in tears of the infected patients, and reports suggest that the ocular surface could serve as a portal of entry and a reservoir for viral transmission. Although, COVID-19 has been clinically associated with mild conjunctivitis, which can be the first and only symptom of the disease, subtle retinal changes like hyperreflective lesions in the inner layers on optical coherence tomography (OCT), cotton-wool spots, and microhaemorrhages have also been reported. It has also been associated with an increased incidence of systemic diseases like diabetes mellitus and Kawasaki disease, which are particularly relevant for ophthalmologists due to their potentially severe ocular manifestations.

INTRODUCTION

The coronavirus disease became a global pandemic in the year 2019 and since then up till now, a lot of research has been done to understand the causative virus – severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) – and the disease itself. All in an effort to create guidelines and develop global standards to provide treatment for those infected by the disease as well as to curtail the spread of the virus.¹

The absence of a pathognomonic symptom with which to detect the disease has resulted in challenges regarding the diagnosis of COVID-19. The disease has a wide range of symptoms which affects almost every organ system in the human body including the gastrointestinal, urinary, and cardiovascular systems.^{2,3} At the early stages of the pandemic, reports of ocular symptoms – such as conjunctivitis – associated with covid-19 began to emerge.⁴ Other prevalent ocular manifestations of COVID-19 include dry eyes, redness, epiphora, and more.⁵

Apart from these ocular symptoms, a separate concern began to rise pertaining to the likelihood of the virus being

transmissible via ocular secretions. In 2003, during the outbreak of the severe acute respiratory syndrome, the causative virus (SARS-CoV) was detected in the tear samples of some SARS patients in Singapore.⁴ Expectedly, similar concerns began to rise concerning the SARS-CoV-2. The human conjunctiva has also been found to be a potential site for SARS-CoV-2 transmission.³

Knowledge about the types and the prevalence of ocular involvement seen in COVID-19 cases can go a long way to help doctors in diagnosing or ruling out COVID-19 infections in sick patients.⁵ It will also help reduce the risk of transmission to the healthcare provider – particularly the ophthalmologist.

This paper discusses the ocular manifestations of COVID-19, the epidemiology and aetiology of these symptoms, possible differential diagnoses, management of these symptoms as well as possible complications.

AETIOLOGY

COVID-19 is a predominantly respiratory disease which is caused by the SARS-CoV-2 virus, a positive sense single-

stranded RNA virus. In animals such as feline and murine species, coronaviruses have been found to cause ocular symptoms including uveitis, retinitis, conjunctivitis, and even optic neuritis.^{3,4} Although occurring among humans that are positive for COVID-19, the ocular manifestations of this disease tend to be mild and infrequent.⁴

The occurrence of these ocular manifestations has been postulated to be due to the presence of ACE2 receptor in the cells of the eye. This ACE2 receptor has been established as the receptor through which SARS-CoV-2 effects its harm on the body.^{4,5} In addition to facilitating the tropism of this predominantly respiratory virus to ocular tissue, the presence of these permissive receptors may also allow the virus to replicate in the eye as well as spread to extraocular tissues, becoming a systemic infection.⁶

Another route of entry of the virus has been found to be via the CD147 receptor. This receptor has been immunohistochemically localised in different human ocular tissues including the corneal epithelium, conjunctiva, etc.⁷ Tear samples taken from COVID-19 patients with dry eye disease have been found to have an increased expression of CD147 receptors.⁷

EPIDEMIOLOGY

The occurrence of ocular manifestations of COVID-19 was found to be between 7-11% in patients who were found to be infected with the disease. No significant correlation was found to exist between ocular manifestations of COVID-19 and the patient's gender or the presence of comorbidities.^{4,5,8,9,15}

OCULAR MANIFESTATIONS OF COVID-19

Although COVID-19 has been primarily classified as a respiratory disease, it affects various organ systems in the body, including the eyes. In some cases, ocular symptoms of Covid-19 have occurred as the primary presenting complaint of infected patients^{9,15} and rarely, as the only symptom of the infection.^{4,10}

Ocular manifestations of COVID-19 have been found to COVID-19 are ocular surface symptoms. However, the disease has been found to affect even the optic nerve.

Some of the major ocular manifestations of COVID-19 are discussed below:

- **Conjunctivitis**

Symptoms of acute conjunctivitis have been found to be some of the most common ocular symptoms associated with COVID-19 infection.^{4,5,6,7,9} Some of these symptoms include ocular irritation, epiphora, chemosis, eyelid swelling, conjunctival hyperemia and congestion.

Conjunctival hyperaemia was found to be one of the most prevalent clinical manifestations of COVID-19 conjunctivitis.^{4,5,8,9,14}

Conjunctivitis, in some cases, has occurred as the initial symptom of the COVID-19 infection.^{6,10,12} Rarely, COVID-19 conjunctivitis has occurred as the only symptom of the infection.^{4,10} At least one case of keratoconjunctivitis has also been reported.¹¹

Symptoms of COVID-19 conjunctivitis were found to be more prevalent among patients with more severe pneumonia or systemic manifestations associated with the infection.^{3,6,12} However, symptoms of COVID-19 conjunctivitis have also been reported as a major ocular manifestation of the infection even in patients with a milder form of the disease.¹⁵

Apart from COVID-19 conjunctivitis, other ocular manifestations of COVID-19 include;

- **Dry eye**

This was found to be among the most prevalent ocular manifestations of COVID-19.^{5,13} However, it has been postulated that the manifestation of this ocular finding may not be directly related to the viral infection and may be as a result of expiratory current being directed towards the eyes due to the use of face masks, accelerating the evaporation of tears and drying out the eyes.⁵ Increased time spent looking at screens during the movement-limitations imposed during the COVID-19 pandemic has also cornea, conjunctiva, and sclera.⁴ Most often, the ocular manifestations of been postulated as another likely theory which could explain COVID-19-associated dry eye.⁵

- **Foreign body sensation**

Foreign body sensation has also frequently been found as a major ocular manifestation of COVID-19.^{4,5,6,13}

- **Episcleritis and Scleritis**

These are relatively rare ocular manifestations which have nonetheless been reported to have occurred in association with COVID-19 infections.^{4,14}

- **Acute Anterior Uveitis**

Has also been reported in association with COVID-19 infection.^{18,19}

- **Neuro-ophthalmological manifestations**

Neuro-ophthalmological manifestations associated with Miller Fisher syndrome and polyneuritis cranialis have been reported in two respective COVID-19 patients. In both cases, the presenting complaint was diplopia. The first patient had fever, malaise and respiratory symptoms before eventually presenting with right internuclear

ophthalmoparesis and right fascicular oculomotor palsy. The second COVID-19-infected patient experienced fever and general malaise prior to presenting with bilateral abducens palsy and areflexia.¹⁶

Optic neuritis has also been reported in patients infected with the virus.⁴ Other neuro-ophthalmological manifestations such as right abducens palsy and papilledema due to raised intracranial pressure secondary to COVID-19-associated multi-system inflammatory syndrome in children (MIS-C) have also been reported.¹⁷

Follicular conjunctivitis, conjunctival hyperaemia, chemosis, and epiphora are the most prevalent ocular symptoms in adults. Optic neuritis, disk oedema, retinal artery occlusions, intraretinal haemorrhages, cotton wool spots, and uveitis as well as neuro-ophthalmology signs and symptoms such as ocular pain, diplopia and myasthenia gravis have all been reported in COVID-19 patients as posterior segment ocular manifestations. Long-term follow-up is required to assess the long-term COVID-19 ocular manifestations that may develop over time and more studies are needed in the geriatric and paediatric populations.¹³

DIFFERENTIAL DIAGNOSES

Symptoms that are similar to COVID-19 conjunctivitis can occur as a result of other disease conditions un-related to COVID-19 infection. Some of these disease conditions include:^{6,20,21}

- Renal failure
- Cardiopulmonary failure
- Carbon dioxide retention
- Influenza virus infection
- Mycoplasma pneumonia-associated mucositis

TREATMENT/MANAGEMENT

As with many viral infections, COVID-19 conjunctivitis is self-limiting and can be effectively managed with supportive and symptomatic care. Barring decreased vision, light sensitivity or excruciating eye pain, it can be managed with a preservative free artificial tear, cold compresses and ophthalmic lubricants. Topical antibiotics can be introduced to prevent or treat superimposed bacterial infections based on the patient's symptoms and risk factors.²²

A study by Chen et al., suggested that the administration of ribavirin eye drop showed gradual symptomatic improvement of COVID-19 conjunctivitis in one patient.¹³ However, it is unlikely to have a long-term clinical importance in a self-limited viral illness and care should be taken not to decrease possible viral load and possible transmission.^{23,13}

Earliest studies suggested that the risk of viral transmission through ocular secretions is low but new large-scale studies are yet to be done and new data are emerging daily as the novel disease is still being understudied. However, the probability of viral transmission through tears has been found to be high in patients with moderate to severe COVID-19. For RT-PCR tear collection, the conjunctival swab remains the gold standard.²⁷

As a precaution, healthcare providers are encouraged to wear proper protections for the eyes, nose and mouth when examining patients as eye care providers may be more susceptible to infection as a result of the nature and proximity of the ophthalmic examination. Slit lamp breath shields should be used and patient counselled to speak as little as possible when sitting in the slit lamp to reduce the risk of transmission of the virus.²⁴

Shared clinic equipment such as tonometers, trial frames, pinhole occluders, B-scan probes and contact lenses for laser procedures are to be thoroughly disinfected and sterilized. Where possible, disposable barrier protections of clinic tools should be used.^{24,25}

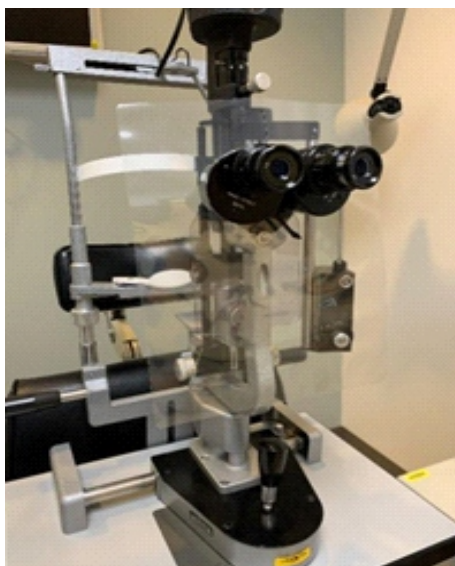
The American Academy of Ophthalmology (AAO) in March 18, 2020 urged all ophthalmologists to provide only urgent or emergent eye care in order to reduce the risk of SARS-CoV-2 transmission and to conserve disposable medical supplies. Although many centres have since resumed elective surgeries and have expanded care on a case-by-case basis following the guideline of the Federal Government.

Protection of Eye Care Providers and Necessary Precautions.

- It was noted that droplets from sneezes can travel up to 6 meters.²⁶ As a result of this, inventive ophthalmic technicians at the Moran Eye Centre developed a slit-lamp shield (pictured below) made by passing two plastic sheets through a laminator without a paper in between and cutting openings for the eyepieces. In like manner, others used old X-ray films when commercially made shields were unavailable.
- Conversations were kept to the barest minimum during the consultation to reduce spread and transmission of the virus.
- Ophthalmic surgeons were urged to take appropriate precautions during the administration of the local anaesthetic because as many as a quarter of patients being injected under sedation develop a severe involuntary sneeze; which is seen more commonly with eyelid injections than with retrobulbar injections.^{27,2}

Sterilization of Equipment

- The slit-lamp shields are disinfected with 70% ethyl



A slit-lamp shield to protect the examiner as designed by Moran Technicians Stein Erickson, Emily Petersen and Anna Reed together with help from others: made by passing two lamination sheets together through a laminator without anything in-between. Results in a rigid shield which can be cleaned with alcohol and reused. Other materials that may be used include used X-Ray films but these do not have the clarity needed.

alcohol after each patient; 70% ethyl alcohol has been shown to reduce coronavirus infectivity.²⁶

- Slit lamps, B-scan probes, and any other tools are also cleaned with 70% ethyl alcohol.
- Goldman tonometers are sterilized with a 10% diluted sodium hypochlorite solution, which inactivates coronaviruses.²⁹

Patient Education

Patient education geared towards prevention and control are pertinent to limiting the spread of disease. As such, in addition to physical distancing and practicing good hand-washing hygiene, patients were urged to adopt behavioural habits aimed at reducing direct touching of the eyes and face. Such habits include; wearing of glasses and sunglasses instead of contact lenses; refraining from the application of cosmetics; and airing out bedsheets, pillowcases, and towels regularly.

PROGNOSIS

Conjunctivitis related to COVID-19 is currently thought to be self-limited and larger studies as well as long-term follow-up of patients with other ocular manifestations following COVID-19 infection are yet to be reported.

COMPLICATIONS

Ophthalmologists need to be vigilant to recognise the different ways by which COVID-19 may affect the eye and periorbital tissues. Other sequelae and/or complications from demyelinating disease and stroke requires multidisciplinary approach to management.

CONCLUSION

Adequate knowledge regarding virus incubation, transmission, and shedding is essential for the reduction of new cases and protection of healthcare professionals. There has been several accounts of eye redness and irritation in COVID-19 patients, thus, suggesting that conjunctivitis is an ocular manifestation of SARS-CoV-2 infection. As such, ophthalmologists may be the first medical professionals to evaluate a patient with COVID-19. Therefore, special care must be taken when examining patients with signs and symptoms of viral conjunctivitis. It is compulsory to investigate the presence of respiratory symptoms that may suggest a potential infection.^{30,31} In addition, wearing eye protection when seeing patients on a daily basis during the pandemic is essential.

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