



Ocular Problems Associated with Coronavirus Disease 2019

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Received May 05, 2020; Accepted May 09, 2020; Online Published June 30, 2020

Abstract

Coronavirus disease 2019 has become a worldwide pandemic caused by the infection of severe acute respiratory syndrome coronavirus 2. The infection of this viral illness may cause several ocular manifestations, such as conjunctival congestion, epiphora, and foreign body sensation. Conjunctival mucosa is thought to be one of the certain mediums of transmission of the disease due to the presence of angiotensin-converting enzyme 2, which acts as an intermediary for the invasion of viruses into host cells. Some recommendations have been made to prevent the spreading of the disease in the course of ophthalmic practices. This review aims to emphasize the ocular problems associated with novel coronavirus disease and lays out the efforts that can be done related to disease prevention.

Keywords: Novel Coronavirus, Severe Acute Respiratory Syndrome, Angiotensin-converting Enzyme, Ophthalmology, Infection

Introduction

Since its first identification around late December of 2019, the Coronavirus disease 2019 (COVID-19) has been reported to have caused soaring morbidities and mortalities in the world's population.¹ Globally, at least as of May 1, 2020, more than 3 million confirmed cases and more than 200 thousand deaths related to COVID-19 have been reported.¹ The World Health Organization (WHO) has determined this disease as a worldwide pandemic.² The pathogen that is known to cause COVID-19 is the severe acute respiratory syndrome coronavirus (SARS-CoV-2), which is a novel type of coronavirus similar to SARS-CoV, which caused an outbreak of severe acute respiratory syndrome (SARS) in 2002-2003.^{3,4} The primary manifestation of SARS-CoV-2 virus infection includes the symptoms of respiratory distress, ranging from mild to severe pneumonia, causing death.^{3,5} Some studies showed several manifestations of ocular involvement among patients with SARS-CoV-2 infection.⁶⁻⁸ SARS-CoV infection is known to occur due to direct or indirect contact with the mucous membranes of the eyes, nose, and mouth.⁹ A study also showed the positive results of the SARS-CoV virus RNA strain found in the tear specimen of SARS patients.¹⁰ However, the literature regarding the involvement of SARS-CoV-2 in ocular disorders is still quite limited. This paper aims to provide an overview of eye disorders associated with COVID-19 and to describe the efforts to be done to prevent the disease.

Microbiology and Pathophysiology of Coronavirus

Coronavirus (CoV) is a virus that is included in the subfamily Coronavirinae, Coronaviridae family, and the order Nidovirales. The term corona comes from the Latin "*corōna*," which means crown, referring to the structural characteristics of the virus with the envelope that is shaped like a crown.^{4,11,12} Viruses that belong to the Coronaviridae family are the viruses with a single-stranded ribonucleic acid (RNA) genome and the size of 26-32 kilobases.^{4,11,12} Coronavirus is known to infect birds and mammals.⁴ In humans, there are at least seven types of coronaviruses that have the potential to be infectious. Three of them cause threatening clinical manifestations, including the SARS-CoV, Middle East Respiratory Syndrome Coronavirus (MERS-CoV), and SARS-CoV-2 itself.^{4,11}

When the virus enters the human body, SARS-CoV binds to the Angiotensin-Converting Enzyme 2 (ACE2) receptor, which is commonly expressed in the lungs, heart, ileus, kidneys, and bladder. During replication, the ACE2 receptor binds to the protein "spike" on the surface of the virus and triggers the protease cleavage in the biosynthesis of the virus in the host cell. In response to the host immunity, activation of the T cell also occurs, which is initiated by the Antigen-Presenting Cells (APCs) in the form of dendritic cells and macrophages. Both of these immune cells are capable of phagocytosis of infected cells, thereby triggering apoptosis of these cells.³

Ocular Manifestation of COVID-19

Several studies have shown SARS-CoV-2 infection with clinical manifestations in the eye. Although ocular manifestations did not commonly become the main

symptoms found among COVID-19 patients, a study found that at least 0.8% of 55,924 cases in China revealed the signs of conjunctival congestion.¹² A case report in China also showed the emergence of eye disorder that occurs in a patient treated in hospital due to COVID-19. On the thirteenth day after the onset of the disease, the patient was found to have pink, watery eyes, and foreign body sensation without any visual disturbance. The patient denied touching the eye with his hand. Eye examination showed conjunctival injection, secretions, follicles in the inferior palpebra, and enlargement of the preauricular lymph glands. Patients also had a positive result of SARS-CoV-2 based on Reverse Transcription-Polymerase Chain Reaction (RT-PCR) examination from conjunctival swab.⁸

The study conducted by Ping and colleagues showed that 12 out of 38 (31.6%) patients treated with COVID-19 indications had symptoms of eye disorders, which included conjunctival congestion, chemosis, epiphora, and appearance of eye secretions. Eleven out of 12 (91.7%) patients were found to have a positive SARS-CoV-2 based on RT-PCR examination from nasopharyngeal swab, but only two of 12 (16.7%) were found to have a positive SARS-CoV-2 based on RT-PCR analysis of conjunctival swab. One patient was found to experience epiphora as an initial symptom of COVID-19.⁶

In a study conducted by Chen et al. it was found that 25 out of 534 (4.68%) COVID-19 patients had conjunctival congestion, 3 of which showed this appearance as their early symptom. Among these patients, it was known that 18 (72%) of them had a history of direct eye contact, and 12 of them did not wash their hands before touching their eyes. The other ocular problems that were most often found included dry eyes (20.9%), blurred vision (12.7%), foreign body sensation (11.8%), and epiphora (10.3%).⁷

The study conducted by Hong et al. assessed subjective eye disorders before and after the patient was confirmed with COVID-19. This study used the Ocular Surface Disease Index (OSDI) and Salisbury Eye Evaluation Questionnaire (SEEQ) and found a statistically significant difference between clinical symptoms before and after COVID-19 confirmed subjects. Fifteen out of 56 (26.8%) patients showed ocular manifestations, which included eye pain, itching, foreign body sensation, watery, red eyes, dry eyes, eye secretions, and floaters. However, RT-PCR examination from the conjunctival swab showed a positive result in only one patient.¹³

Is SARS-CoV-2 Ocular Transmission Possible?

Despite the evidences of ocular manifestations related to COVID-19 and positive findings of SARS-CoV-2 in tears, the mechanism by which the virus can end in the eye is still unclear. Manifestations that occur also do not clearly describe whether the symptoms appear due to primary

infection SARS-CoV-2 or occur as the comorbidity of the current COVID-19 infection. The positive findings of SARS-CoV-2 in conjunctival swab also does not necessarily prove the existence of viral replication and transmission through the conjunctival mucosa.

Several hypotheses suggested that the ocular manifestations that occur are related to the conjunctival mucosa being the site of SARS-CoV-2 inoculation, originating from splashes of infected patients' droplets, hand-to-eye contact, or aerosols transmission directly to the conjunctiva.^{14,15} Other hypotheses also stated the possibility of transmission originating from the migration of the nasolacrimal duct in patients with upper respiratory tract infections or transmitted hematogenously through the lacrimal gland.¹⁴ In a study, it was concluded that ACE2 expression was found to be positive and could bind as the SARS-CoV virus receptor in conjunctival epithelial cells, conjunctival fibroblast cells, and corneal epithelial cells.^{8,16} Unfortunately, currently, there are no studies that can explain the relationship between ACE2 expression in the eye associated with SARS-CoV-2 transmission.

A study done by Seah and colleagues stated that the risk of SARS-CoV-2 transmission through the eyes was quite low, because the virus was not detected based on the viral culture and RT-PCR examination in the tears of confirmed COVID-19 patients.¹⁷ Previous studies also showed a low positive number of viruses found in the results of RT-PCR from conjunctival swab.^{6,8,13,18} Nevertheless, based on the theories and findings that have been presented, we cannot easily deny that there is still a potential ocular transmission of SARS-CoV-2 through the eyes.

Prevention of COVID-19 through Eye

The COVID-19 disease shows diverse clinical manifestations. Most patients show nonspecific symptoms, including fever, coughing, and shortness of breath.⁵ This pandemic has become a challenge, especially for Health Care Workers (HCW). The incidence of COVID-19 among HCW is quite common, indicating a high risk of transmission among HCW.¹⁹ During the eye examination, doctors often have to examine in very close contact with the patient. In fact, on examinations such as direct funduscopy, there is almost no distance between the doctor and the patient. Some recommendations that can be made relating to the prevention of SARS-CoV-2 transmission related to the eyes are stated below:^{15,20}

- Use personal protective equipment suitable for eyes (protective goggles or breath shield), nose and mouth (at least surgical masks and N95 or its equivalent especially when performing medical procedures with potential aerosol contamination), and hands (standard medical gloves) when examining patients

- Identify the initial risk of SARS-CoV-2 exposure by asking for symptoms and signs of respiratory distress in COVID-19, travel history, or history of contact with people with high-risk transmission of SARS-CoV-2 in the last 14 days
- Advise patients to wear a mask and refrain from speaking during eye examinations requiring close contact between doctor and patient
- Repeated use of eye drops for diagnostic purposes can be done by taking care that the tip of the eye drops does not touch the surface of the eye and its surroundings
- Prioritize the use of teleconsultation services to prevent direct contact with patients whenever possible and if the patient is not in an ophthalmic emergency condition (red eyes, sudden blurred vision, chemical trauma/penetrating/ blunt, and unbearable eye pain)
- Always do the cleaning and carry out routine disinfection of the environment and the examination instruments used in each patient. Recommended disinfection fluids include alcohol solution with the concentration not less than 70% and diluted bleach (5 tablespoons for 1 gallon of water).

Acknowledgments

None.

Authors' Contribution

All authors pass the four criteria for authorship contribution based on the International Committee of Medical Journal Editors (ICMJE) recommendations.

Conflict of Interests

The authors declared no potential conflict of interests with respect to the research, authorship, and/or publication of this article.

Funding/Support

The authors received no financial funding or support for the research.

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