



Conjunctivitis and other ocular manifestation following COVID-19; updated information about transmission of COVID-19 by eye

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Abstract

Coronavirus disease 2019 (COVID-19) was reported in Wuhan, in late December 2019 and was became a pandemic health problem worldwide. In this review, the current evidence related to the ocular transmission of SARS-CoV-2 and its common manifestations was studied. According to this review, 7% to 69.4% of patients had at least an ocular symptom following COVID-19. Ocular symptom are bilateral or unilateral conjunctivitis, increased secretion, eye itching and foreign body sensation, epiphora, dry eye, conjunctival congestion, eye pink, conjunctival hyperemia, and chemosis. SARS-CoV-2 particles were found in tears and conjunctiva. Therefore, the transmission of COVID-19 by conjunctiva is possible. Then, it is essential to wear eye shield to protect against developing ocular involvement by COVID-19 because personal glasses and contact lenses cannot protect from COVID-19.

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Introduction

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) like other viruses in the Coronaviridae family, is highly contagious and in a short time, lots of countries became infected with SARS-CoV-2; Likewise, the World Health Organization (WHO) on March 11 declared it as a global pandemic (1,2). In fact, SARS-CoV-2, known as coronavirus disease 2019 (COVID-19), has spread from Wuhan, China, and affected more than 33 million people and caused more than one million deaths (3).

Symptoms of the COVID-19 include fever and cough, shortness of breath, and pneumonia, which in most patients appear as ground glass in imaging radiology. In laboratory studies in most patients, lymphocytopenia, increased C-reactive protein and hepatic aminotransferases can be observed. Severe fatigue, gastrointestinal symptoms, and radiological appearance in

Key point

Ocular symptoms are not uncommon in COVID-19. It is essential to protect eyes and lacrimal glands from SARS-CoV-2. Conjunctivitis is the most common symptom in patients with COVID-19. It should be noted that the transmission of COVID-19 by conjunctiva is possible. Then, it is essential to wear eye shield to protect against developing COVID-19.

the form of septal thickening have also been reported in some studies (4,5).

The manifestations of COVID-19 are different in age and gender. In 25% of cases, COVID-19 progresses to respiratory failure. Mortality rates are high in patients who require ventilators. Therefore, initial control is necessary to prevent the progression of respiratory symptoms to acute respiratory distress syndrome (ARDS) and to prevent mortality (6). COVID-19 can affect any part of the body (7). In this review, the current evidence associated with the ocular



manifestations and the transmission of SARS-CoV-2 was studied.

Methods and Materials

A structured review was done by 10 Nov 2020, using PubMed, Science Direct, Scopus and Google Scholar on COVID-19, SARS-CoV-2, novel coronavirus disease 2019 and eye, ocular, and ophthalmology. This review included all the published studies related to ocular manifestation after SARS-CoV-2 infection through the eye. In this review, a total of 763 studies were reviewed.

Conjunctivitis

According to some research, keratoconjunctivitis can be the first clinical display of the COVID-19 (8-10). Pirraglia et al showed that 7% of patients with COVID-19 developed bilateral conjunctivitis without corneal sensitivity. In their study performed on 46 patients, retinal involvement following SARS-CoV-2 was not observed. It is suggested to check ophthalmologic status of the COVID-19 patients especially if admitted to the intensive care unit (ICU) (11).

The presence of conjunctivitis was reported previously in coronavirus infections (12). The large study on 1099 patients presented nine cases of conjunctival congestion following COVID-19 in China (13). SARS-CoV-2 can survive on the ocular surface more than the nasopharynx. Colavita et al reported a case with conjunctivitis that lasted about 20 days (14). One potential treatment for conjunctivitis is chloroquine and its other derivatives such as hydroxychloroquine, however it is important to know hydroxychloroquine can cause retinal toxicity as well (15).

In a systematic review and meta-analysis done by Cao et al, the primary outcomes were the prevalence of conjunctivitis and the positive rate of conjunctival swab samples. The findings were 8% for the prevalence of conjunctivitis and 3% for the positive rate of conjunctival swab samples. The frequent ocular symptoms were increased secretion, eye itching and foreign body sensation (16). According to the American Academy of Ophthalmology, SARS-CoV-2 can lead to mild follicular conjunctivitis in patients with COVID-19 (17).

Other ocular manifestations

Other manifestations are itching, conjunctival secretion, foreign body sensation, epiphora and dry eye. Ocular manifestations are reported to be 0.5% to 32% (18). Marinho et al reported four new cases of retinal lesions of microhemorrhages and cotton wool spots (19). A novel coronavirus can cause various ocular infections in animals such as conjunctivitis, retinitis, optic neuritis and anterior uveitis which have been approved in murine and feline models (20). Eye involvement is more likely to be found in severe form of COVID-19, while there are no significant differences between gender and age of patients. The youngest patient with COVID-19 who had conjunctival congestion and eyelid dermatitis was a 34-month-old

boy (21).

In a study conducted by Rokohl et al, 69.4% of patients had at least an ocular symptom following COVID-19 and the most frequent symptoms were as follows: burning sensations in 36.1% of the patients, epiphora in 34.3% of the patients and eye pink in 25.9% of the patients showing conjunctivitis occurred 1.96 days following the onset of COVID-19. According to the study by Rokohl et al, ocular involvement in patients with COVID-19 was underestimated (22).

COVID-19 is associated with conjunctivitis, retinal changes, cotton-wool spots, and microhemorrhages. Due to prone position in some patients with COVID-19, it is possible that intraocular pressure will be elevated and acute ischemic optic neuropathy may happen. However, ocular surface disorders after a long stay in ICU are possible. However, the risk of retinal toxicity following the use of antimalarials such as hydroxychloroquine and chloroquine, and interferons, interleukin-1 and interleukin-6 inhibitors, and lopinavir-ritonavir is still controversial (23).

In a study by Ma et al, of a total of 216 pediatric patients, 49 patients (22.7%) showed various ocular manifestations including conjunctival discharge, eye rubbing and conjunctival congestion. However, children with cough were more likely to develop ocular symptoms. Ocular symptoms were typically mild, and children recovered easily (24). In a study by Hong et al, 27% of the patients with COVID-19 had ocular symptoms. They concluded that ocular symptoms are common in patients with COVID-19 and may present before the onset of respiratory involvement (25).

Transmission

In the review study of Emparan et al, viral particles can be found in tears and conjunctiva. Therefore, the transmission by conjunctiva is remained controversial (26). Due to not wearing eye shield in practice by practitioners, initial protection is easily missed. In addition, there is no suggestion to use eyewear for medical issues. Hence, it is essential to assess the practitioner for developing ocular involvement by COVID-19 (27).

The eye surface and tear maybe are potential places for SARS-CoV-2 colonization. Additionally, COVID-19 transmission should not be ignored through this part of body, that is why respiratory viruses such as influenza virus were reported in the nasolacrimal tissues (28). It is useful to apply enough personal protective equipment in the practice to be protected. Moreover, personal glasses and contact lenses cannot protect from COVID-19 (29).

In Thailand as second place regarding the report of COVID-19, eye involvement never reported. However in China, Xia et al reported the ability of COVID-19 to affect the ocular surface. COVID-19 can cause conjunctivitis. It is possible that SARS-CoV-2 be secreted into tears via the eccrine gland (30). Protective eyewear can directly

prevent conjunctiva from respiratory droplets (31). Xia et al, isolated SARS-CoV-2 virus in tears of patients with COVID-19 (32). Global eye care needs more than ever evidence-based findings to take specific and integrated approach in the community (33).

There are two theories to develop conjunctivitis including hand-eye contact or transmission by aerosol contacts with the conjunctiva. This fact rings a bell to all health care workers involving in close contact with patients. It is recommended that practitioners caring of patients potentially with COVID-19 wear eye shield equipment to protect the eyes (34). Willcox et al, checked the hypothesis “ocular surface is a site of infection with SARS-CoV-2”. They found SARS-CoV-2 under epithelia of the ocular surface and SARS-CoV-2 is transmitted by person-to-person contact via airborne droplets, or through contact with contaminated surfaces. However the study revealed that coronavirus infection associated with conjunctivitis is rare and a few studies report conjunctivitis following COVID-19. There are a few SARS-CoV-2 in the conjunctiva swabs or tears. Willcox et al indicated that the likelihood of infection by conjunctiva is low but possible and rare (35). It is controversial but worth considering whether the SARS-CoV-2 is transmitted by tears and ocular surface. Several mechanisms for this root of infection focus on the nasolacrimal system (36).

COVID-19 is highly contagious and ophthalmologists are at risk due to some reasons like the contact with conjunctiva, close distance between ophthalmologists and patients during visit, contact with patients’ tears (37).

In a study by Wu et al, 31.6% of the COVID-19 patients had ocular involvement (conjunctival hyperemia, epiphora, and chemosis) especially in severe cases. Regarding possible transmission by eye surface, 5.2% of patients had positive findings for SARS-CoV-2 in their conjunctiva and nasopharyngeal specimens (38). Shemer et al indicated that patients with COVID-19 are more likely to complain of pink eye (25%) and foreign body sensation (31.3%) (39).

It is rational that all health care providers should consider tears to be potentially infectious (40). There is also some evidence showing that ocular manifestations occur in the severe form of the COVID-19 (41). Ocular symptoms may be the first signs of the COVID-19. The probably role of conjunctiva in the transmission process makes a long-term commitment to consider hygienic recommendations and consequently the use of personal protective equipment (PPE) (42). In a study by Zhou et al, 3 out of 121 patients were positive reverse transcription-polymerase chain reaction (RT-PCR) in conjunctiva swabs (43).

Conclusion

Accordingly, 7% to 69.4% of patients following COVID-19 develop at least an ocular symptom including bilateral or unilateral conjunctivitis, increased secretion, eye itching and foreign body sensation, epiphora, dry eye,

conjunctival congestion, eye pink, conjunctival hyperemia, and chemosis. SARS-CoV-2 was found in tears and conjunctiva. Therefore, the transmission of COVID-19 by conjunctiva is possible. Then, it is essential to wear eye shield to protect against developing ocular involvement by COVID-19 because personal glasses and contact lenses cannot protect from COVID-19. It is suggested to run further studies to check the contamination of tear and conjunctiva specimens with SARS-CoV-2.

Authors’ contribution

MM and NSA were the principal investigators of the study. NG and SMAH participated in preparing the concept and design. MM and NSA revised the manuscript and critically evaluated the intellectual contents. All authors participated in preparing the final draft of the manuscript, revised the manuscript and critically evaluated the intellectual contents. All authors have read and approved the content of the manuscript and confirmed the accuracy or integrity of any part of the work.

Conflicts of interest

The authors declare that they have no competing interests.

Ethical considerations

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

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