OCULAR FINDINGS IN COVID-19 PATIENTS: A SYSTEMATIC REVIEW

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ABSTRACT

The World Health Organization (WHO) has declared the 2019–20 coronavirus outbreak a Public Health Emergency of International Concern (PHEIC). Covid-19infection is an ongoing pandemic with high morbidity and mortality, spread from one infected personto another through respiratory airway droplets.Covid-19circulatesin many organs, including the heart, kidneys, brain, etc.Ocular symptoms, along with other symptoms, may help diagnose COVID-19. Covid-19 ocular signs of dry eyes, weeping, itching, redness, eye discomfort, foreign body feeling, elevated CRP, Procalcitonin (PCT), and erythrocyte sedimentation rate (ESR) levels, indicating an immunologic response and disease severity. There was a positive correlation between high temperature and visual symptoms.

Keywords: Covid-19;Conjunctivitis; Ocular Disease; Visual Impairment
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INTRODUCTION

The World Health Organization (WHO) has declared the 2019–20 coronavirus outbreak a Public Health Emergency of International Concern (PHEIC). Evidence of local disease transmission was found in many countries across all six WHO regions as of March 7, 2020.[1]The World Health Organization announced on February 11, 2020, that " Covid-19" will be the official name of the disease. "Co" stands for "corona", "Vi" for "virus", and "D" for "disease", while "19" is for the year because the outbreak was first identified on December 31, 2019.[2]

Covid-19 infection is an ongoing pandemic characterized by high morbidity and mortality. It needs urgent to identify clinical and biological predictors of severity and mortality associated with Covid-19 infection for the judicious use of limited resources.[3]There have been more than 16 million cases and more than 500,000 deaths reported worldwide. The rate of new infections appears to be outpacing the scale of public health preparedness and response, especially in countries with limited economic capacity.[4]

This infection spreads Covid-19 to another through respiratory droplets when coughing and sneezing. The incubation time is generally between 2-14 days, with an average of 5 days.[5]This disease caused severe acute respiratory syndrome coronavirus 2 (SARS-

CoV-2), previously known as the 2019 novel coronavirus (2019-nCoV). [6,7]

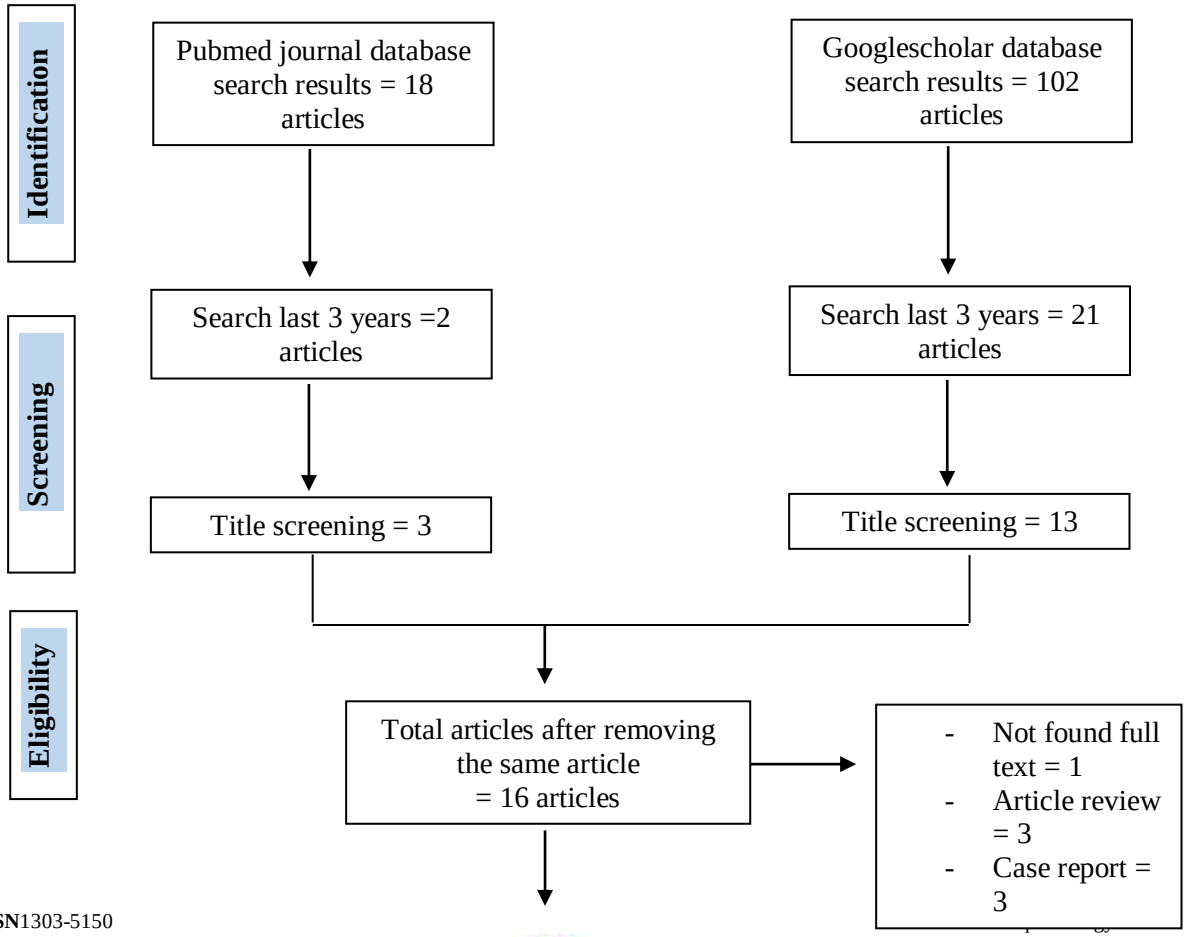
The virus accesses host cells via angiotensin-converting enzyme-2 (ACE-2). Angiotensin-converting enzyme-2 is found in various body organs and abundant in type II alveolar lung cells. This mechanism explains why the lungs are the most affected organs. The density of ACE2 determines the severity of the disease.[5]As the alveolar disease progresses, severe acute respiratory syndrome (SARS) develops, leading to respiratory failure and death. In addition, Covid-19can circulate to many organs, such as the heart, kidneys, brain, etc.[5]This article discusses the ocular findings of patients with Covid-19.

METHODS

The data for this systematic review were culled from full-text English publications published in the preceding threeyears (2019-2022). This study aims to determine ocular findings in COVID-19 patients.The databases that we utilized to produce this article are Pubmed and Google Scholar. The study comprised both clinical trials and randomized clinical trials.Under the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) paradigm, the researchers initially input keywords into each database for this study.

The phrases "Ocular Finding" and "Covid-19" were used in the search, the words: "ocular", "diagnosis", "signs and symptoms", "covid 19", "covid 19 vaccines", "covid 19 serotherapy", "covid 19 nucleic acid testing", "covid 19 serological testing", "covid 19 testing", "sars cov 2", "severe acute respiratory syndrome coronavirus 2", "ncov", "2019 ncov", and "coronavirus".

From 2012-2022 we found 120 articles, and 16 were matched. Finally, we received 9 articles shown in figure 1, which will be discussed during the discussion **(Table 1)**.



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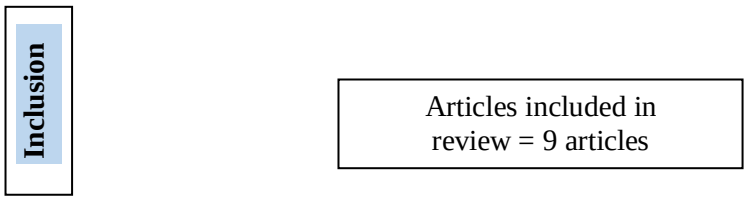

Figure 1. Article search flowchart

RESULT

Zhang showed that two COVID-19 patients (2.78%) had conjunctivitis, and one patient's ocular discharges contained SARS-CoV-2 RNA fragments by RT-PCR. Our data suggest SARS-CoV-2 infection via the ocular surface is rare, although occupational exposure through the eyes is a plausible pathway.[8]Patients with novel coronavirus pneumonia (NCP) of both the common and severe types, a total of twenty-one, were included in the study. The only patient who had conjunctivitis was the one who had two samples of tear and conjunctival secretions taken from him. Both of these samples produced positive findings when run via RT-PCR. There was no positive result among any fifty-eight samples from different patents.[9]

Ping conducted a study with 38 patients, and 12 showed ocular signs consistent with conjunctivitis. These manifestations included conjunctival hyperemia, chemosis, epiphora, or elevated secretions. According to the results, patients who experienced ocular symptoms were more likely to have higher white blood cell and neutrophil counts and higher levels of procalcitonin, C-reactive protein, and lactate dehydrogenase of univariate analysis.[10]

Bostanci showed that at least one visual anomaly was seen in 21.5% of the patients. The most frequent results were hyperemia (n = 20), epiphora (n = 9), increased secretion (n = 6), chemosis (n = 3), follicular conjunctivitis (n = 2), and episcleritis (n = 2). Hyperemia was the most prevalent finding. Photophobia was the one that was seen most often (n = 15).[14] Abrishami et al. (2020) study,in44 (31%) patients who showed conjunctival hyperemia, and 22 (15.5%) had chemosis on the first ophthalmologist examination. 41 (28.9%) had conjunctival hyperemia, 22 (15.5%) chemosis, 11 (7.7%) cataract, and 9 (6.3%) diabetic retinopathy. Patients with ocular involvement showed greater blood urea levels at admission than those without.[15]

The fourth study showed that 15 (56%) of the 27 patients experienced respiratory symptoms, while 8 (30%) had gastrointestinal symptoms. All patients had positive nasopharyngeal swabs for COVID-19 upon admission; 7 (26%) tested negative on the second swab, and 20 remained positive. Four individuals had conjunctivitis-like ocular symptoms (15%). One and 2 asymptomatic individuals were positive for COVID-19 on the first conjunctival swab; 2 turned negative on the second and 1 on the third.[11]

Ocular signs were seen in 39 (7.8%) of the evaluated individuals. Most patients in COVID-19 were male, and 20, which is twenty percent of the total, had a history of having various comorbidities. The patients' majority was hyperemia (13/33.3%), eye discomfort (9/23.1%), epiphora (8/20.5%), a burning feeling (4/10.3%), and photophobia (2/5.1%) individuals.[12]Initial COVID-19 ocular symptoms may include conjunctival congestion. Frequent hand-eye contact may cause COVID-19 conjunctivitis. During COVID-19 outbreaks, ophthalmologists should screen individuals with conjunctival congestion. Eye-care equipment and eye-protection education are crucial.[13] Other studies showed that 23% were infected in Wuhan, 32 patients (or 57%) were infected in the community, 10 patients (18%) were of unknown origin, and 1 patient (2%) was a physician who a confirmed patient most likely infected.[16]

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Table 1. The literature included in this study

Author	Origin	Method	Sample Size	Period	Result
Zhang, 2020[8]	China	Cross-sectional study	102 patients	December 30, 2019, and February 7, 2020	The prevalence of SARS-CoV-2 infection via the ocular surface in the general population is exceedingly low, suggesting that this transmission route is not standard.
Jianhua, 2020[9]	China	A prospective interventional case series study	30 patients	January 26, 2020, to February 9, 2020	Patients with novel coronavirus pneumonia (NCP) of both the common and severe types, a total of twenty-one, were included in the study. The only patient who had conjunctivitis was the one who had two samples of tear and conjunctival secretions taken from him. Both of these samples produced positive findings when run via RT-PCR. There was no positive result among any fifty-eight samples from different patents.
Ping, 2020[10]	China	Cross-sectional study	38 patients	February 9 to 15, 2020	12 of 38 patients (31.6%) experienced conjunctival hyperemia, chemosis, epiphora, or elevated secretions. Patients with ocular symptoms had more significant white blood cell and neutrophil counts and higher levels of procalcitonin, C-reactive protein, and lactate dehydrogenase. 11 of 12 patients with ocular abnormalities reported positive SARS-CoV-2 RT-PCR findings from nasopharyngeal swabs. 2 (16.7%) reported positive conjunctival and nasopharyngeal RT-PCR results for SARS-CoV-2.
Paola, 2020[11]	Italy	Prospective observational case series study	27 pediatric patients	March 16 to April 15, 2020	15 (56%) of the 27 patients experienced respiratory symptoms, while 8 (30%) had gastrointestinal symptoms. All patients had positive nasopharyngeal swabs for COVID-19

					upon admission; 7 (26%) tested negative on the second swab, and 20 remained positive. Four individuals had conjunctivitis-like ocular symptoms (15%). One symptomatic and 2 asymptomatic individuals were positive for COVID-19 on the first conjunctival swab; 2 turned negative on the second and 1 on the third.
Nissar, 2022[12]	Qatar	Retrospective study	500 patients	March to May 2021	Thirty-nine individuals (7.8%) had ocular symptoms. 200 (20%) COVID-19 patients have additional comorbidities. Our patients exhibited hyperaemia (13 [33.3%]), eye discomfort (9 [23.1%]), epiphora (8 [20.5%]), burning sensation (4 [10.3%]), and photophobia (2 [5.1%]). Ocular symptoms did not vary by gender or comorbidities (p >.05).
Liwen, 2020[13]	China	Retrospective study	535 COVID-19 patients	February 1 to March 1, 2020	Congestion of the conjunctiva is one of the COVID-19-related ocular symptoms, and it may be one of the first symptoms someone experiences. One of the risk factors for conjunctival congestion in COVID-19 individuals may be frequent hand-eye contact. During the outbreak of COVID-19, it is recommended that ophthalmologists do screenings on individuals with conjunctival congestion. In addition, it is of the utmost importance to make eye care equipment available and to improve education on eye protection.
Bostanci, 2020[14]	Turkey	Cross-sectional study	93 COVID-19 patients	March 1, 2020, and April 30, 2020	21.5% had eye abnormalities. Hyperemia (20), epiphora (9), increased secretion (6), chemosis (3), follicular conjunctivitis (2), and episcleritis

					(2) were the most prevalent results. Photophobia was most prevalent (n 15). Patients with ocular involvement had higher neutrophil counts (p = 0.001) and CRP, PCT, and ESR values (p 0.001). Patients with ocular symptoms had decreased mean lymphocyte counts (p = 0.001). The ocular involvement group had a greater mean age and number of patients with fever exceeding 37.3 °C (p = 0.001, p = 0.006).
Abrishami, 2020[15]	Iran	Cross-sectional study	142 patients	No data	44 (31%) patients showed conjunctival hyperemia, and 22 (15.5%) had chemosis on the first ophthalmologist examination. 41 (28.9%) had conjunctival hyperemia, 22 (15.5%) chemosis, 11 (7.7%) cataract, and 9 (6.3%) diabetic retinopathy. Patients with ocular involvement showed greater blood urea levels at admission than those without.
Hong, 2020[16]	China	Cross-sectional study	56 patients	January 19 to February 29, 2020	Thirteen patients (23%) were infected in Wuhan, 32 (57%) were community-infected, 10 (18%) were of unknown origin, and 1 (2%) was presumably infected by a confirmed case. When contacting confirmed patients, three patients wore masks. 15 (27%) experienced exacerbated ocular symptoms, and 6 (11%) had prodromal symptoms before the illness started. Before and after COVID-19, OSDI and SEEQ mean scores differed significantly (p 0.05).

DISCUSSION

The percentage of COVID-19 patients who exhibit ocular symptoms and signs might vary from less than one percent to more than thirty percent.[10,17]Covid-19 ocular symptoms are milder in children than in adults. SARS-CoV-2 transmission via tears may be conceivable, even in individuals without ocular disease.[11]Patients often presented with conjunctivitis as their primary ocular condition.[16,18]Burning eyes, a foreign body sensation in the eyes, photophobia, clear watery discharge, eyelid edema, conjunctival hyperemia, conjunctival injection, pseudomembranous and hemorrhagic conjunctivitis, follicular kerato-conjunctivitis, and corneal sub-epithelial infiltrates are some of the various ophthalmic features that have been described in Covid-19.[18,19]

At this time, it is believed that COVID-19 conjunctivitis is self-limited. There have been no significant investigations or long-term follow-ups of COVID-19 patients with ocular signs. On a global scale, we are engulfed in a precarious situation marked by ebbs and flows of infectious diseases. The international response to the infection has been somewhat disjointed, and the vaccine administration has been unbalanced. As a result, the hope that out of the suffering will come joy and that new strengths will emerge from recognizing the weaknesses of administrations worldwide is a distant hope at this point.[9,20]

Initial Covid-19 ocular symptoms may include conjunctival congestion. Frequent hand-eye contact may cause Covid-19 conjunctivitis. During Covid-19 outbreaks, ophthalmologists should screen individuals with conjunctival congestion. Eye-care equipment and eye-protection education are crucial.[13] Bostanci showed that patients who presented with visual signs had higher ESR levels. In most cases, the ESR will rise within twenty-four hours after the inflammatory process. ESR, like CRP, is not a specific test, which may be a helpful tool in diagnosing and treating some specific conditions, such as inflammation or infection. Still, it does not provide a definitive answer.[14,21]

Patients diagnosed with COVID-19 have been reported to have epiphora as one of their first symptoms. Epiphora owing to inflammation of the conjunctiva is the working diagnosis for this condition. To this day, there has been no record of infection directly affecting the nasolacrimal system of the lacrimal sac.[17]Patients who were elderly seemed to have a greater likelihood of having ocular problems. This might be a secondary effect of the age-related changes that have already taken place in the ocular tissues of the elderly population, such as dry eye illness, malfunction in the meibomian glands, or infestation by Demodex. Because of the documented breakdown in communication between the innate and adaptive immune systems that occur with aging, it is reasonable to anticipate that ocular issues may become more severe in older persons.[22]

There is a lack of understanding of the mechanism behind a dry eye or a foreign body feeling in COVID-19 patients, and these symptoms are not directly related to SARS-CoV-2. The prevalence of dry eye during the COVID-19 outbreak could have been attributable to people wearing face masks and directing expiratory airflow into their eyes and is particularly likely to have been the case when masks were not fitted tightly against the face and nose.[23]

The constant brushing of air on the eye's surface accelerates the natural process by which tears evaporate, which may lead to dry eye symptoms. The symptoms may be more prevalent and noticeable in those with a history of dry eye or a low-quality tear film. Dry eye signs may become even more severe when patients are prevented from using lubricating products out of concern that they would contaminate their hands or medicine containers.[23]

The pathophysiology of the SARS-CoV-2 virus, as well as the organ manifestations of the virus, are not entirely known. Cytokine storm and the ability of the virus to evade cellular immune responses are both thought to play essential roles in the severity of Covid-19. Individuals with Covid-19 with ocular signs had very high CRP, PCT, and ESR levels. This mechanism may be because the host's active immunological response and the severity of the illness led to these findings and may help

to explain, at least in part, the positive correlation between high temperature and ocular symptoms.[14,24]

Lymphocytopenia and elevated neutrophils indicated a bad prognosis. Both of these symptoms represent an intensified inflammatory process. Patients in our study with a higher ratio of neutrophils to lymphocytes seemed to be at a greater risk of developing ocular symptoms. They may also be a secondary effect of the severity of the illness, which is characterized by a broad, aggressive inflammatory response.[14]SARS-CoV-2 patients should be sent to an ophthalmologist for papilledema evaluation because there have been reports of elevated intracranial pressure associated with extensive inflammation and dural venous sinus thrombosis.[25]

Because of their frequent and intimate contact with patients, ophthalmologists are more likely to contract SARS-CoV-2. There is a risk of transmission, and ophthalmologists should adhere to the recommendations of wearing eye-protective gear in addition to face masks and other protective devices during clinical examinations. Although the transmission of SARS-CoV-2 via tear is not unlikely and the mechanism is uncertain, there exists a risk of transmission.[8,26]Regarding contacts with asymptomatic COVID-19 patients, this is of the utmost importance.[27]

CONCLUSION

Ocular symptoms in confirmed COVID-19 patients often presented with conjunctivitis as their primary ocular condition:dry eyes, weeping, itching, redness, eye discomfort, and foreign body feeling should evaluate as ocular covid-19.

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