



## Research Article

# Ocular manifestations in COVID-19 Patients at Dr. Wahidin Sudiro Husodo General Hospital Mojokerto during January – June 2021

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## ARTICLE INFO

**Submitted** : 21<sup>st</sup> January 2023  
**Accepted** : 28<sup>th</sup> June 2023  
**Published** : 27<sup>th</sup> July 2023

### Keywords:

conjunctivitis, corneal ulcer, COVID-19.

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## ABSTRACT

Coronavirus Disease (COVID-19) is a respiratory infection caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). SARS-CoV-2 can be found in ocular organs through direct inoculation, migration via the nasolacrimal duct, or hematogenous. This study aims to determine the clinical manifestations of eye disease in COVID-19 patients at Dr. Wahidin Sudiro Husodo Mojokerto General Hospital from January-June 2021. A cross-sectional retrospective observational study by collecting secondary data on patient medical records. The research sample was all outpatients and inpatients with a positive PCR test for COVID-19 who were consulted by an ophthalmologist at Dr. Wahidin Sudiro Husodo General Hospital Mojokerto in January-June 2021. A total of 861 cases of patients with positive PCR tests for COVID-19, a total of 67 patients were consulted to eye specialists with a median age of 42.6 years. Among 67 patients, 59 (88%) showed symptoms of conjunctival injection, 8 patients (12%) ciliary infusion with 7 patients diagnosed with keratitis, and 1 patient with ulcer redness. In conclusion, the main eye manifestation most commonly found in COVID-19 patients is conjunctivitis which is characterized by conjunctival hyperemia.



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### INTRODUCTION

Conjunctival hyperemia is associated with a multitude of etiologies that cause dilation of the microvasculature, resulting in a reddish appearance of the conjunctival tissue. Clinically, it is primarily a nonspecific sign associated with seasonal allergens, ocular surface infections, fatigue, and even underlying systemic diseases in some cases. The etiologies causing conjunctivitis can be distinguished into infectious or non-infectious. Viral conjunctivitis accounts for up to 80% of acute conjunctivitis cases, with Adenoviruses causing an estimated 90% of cases. Geographical considerations can help in elucidating specific serotypes of adenovirus that infect populations in the area. Less common origins of viral conjunctivitis are attributed to herpes zoster virus (HSV), Varicella-zoster virus (VZV), and *Molluscum contagiosum* (RB Singh., et al 2021).

Coronavirus Disease (COVID-19) is a respiratory infection caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). SARS-CoV-2 can be found in ocular organs through direct inoculation, migration via the nasolacrimal duct, or hematogenous. (Seah I, Agrawal R, 2019). Clinical manifestations of the eye have been found in the form of conjunctivitis and corneal ulcers (Sen et al, 2021). These manifestations can occur early or mid-course of the disease. Currently, the therapy given is in the form of conjunctivitis and corneal ulcers due to viral infections in general. Currently, there is no specific treatment for viral conjunctivitis. Symptomatic relief may be achieved with cool compresses and artificial tears. For severe cases of conjunctivitis and keratitis, topical corticosteroid drops are prescribed for the relief of symptoms caused by inflammation. However, prolonged use of corticosteroids

increases the risk of adverse effects (Skevaki, C.L., et al. ,2011).

A meta-analysis study involving a total of 16 studies with 2347 cases of patients confirmed positive for COVID-19, stated that 11.64% had ocular manifestations. Symptoms were ocular pain (31.2%), discharge (19.2%), hyperemia (10.8%), and follicular conjunctivitis (7.7%). 6.9% of patients with severe pneumonia are accompanied by ocular manifestations. Covid-19 RNA virus was detected in ocular specimens in 3.5% of patients. Ocular manifestations in patients with COVID-19 with the most common manifestation being conjunctivitis of which 2.78% showed conjunctival congestion. Ocular manifestations in some cases were found at the beginning followed by other respiratory manifestations but some appeared in the middle of the course of the disease. The eyelids, conjunctiva, and cornea are parts of the eye organs that are exposed directly to free air so that they become the first transmission mechanism, namely the direct inoculation site of the droplets that carry the virus (Aggarwal K et al, 2019). Therefore, this study aims to determine the clinical manifestations of eye disease in COVID-19 patients at Dr. Wahidin Sudiro Husodo Mojokerto General Hospital from January-June 2021.

### METHODS

A retrospective cross-sectional, single-center study was conducted between January to June 2021 at dr Wahidin Soedirohusodo Mojokerto. Dr Wahidin Soedirohusodo General Hospital is a general tertiary hospital in East Java as a referral hospital for COVID-19 cases. Data were collected from the hospital records of ocular history and external ocular examinations. Visual acuity and slit lamp examinations were performed for the patients. Total sampling was all cases of COVID-19 PCR-positive patients,



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that consulted to ophthalmologist. The inclusion criteria were as follows: over 18 years of age, patient with positive reverse transcriptase-polymerase chain reaction (RT-PCR) test from nasopharyngeal swab for SARS-CoV-2, hospitalized due to COVID-19, and ability to give verbal consent. Those patients admitted to the intensive care unit, unable or unwilling to give verbal consent, and unable to adequately report previous eye symptoms due to general health status, patients with a history of allergic conjunctivitis, dry eye syndrome, glaucoma, and immunodeficiency were excluded. Ethical approval for this study was obtained from Dr. Wahidin Sudirohusodo General Hospital No.20/KEPK-RSWH/EA/2021.

## RESULTS

### Distribution of clinical manifestation in COVID-19 patients

The demographic data and systemic history of the patients admitted on different dates were collected from hospital records. A total of 67 patients were included in this study. The median age of the patients was 42.6 years (range: 6–69 years); 39 (58.21%) patients were male and 28 (41.79%) were female. Patients with the asymptomatic stage were screened for COVID-19 because of contact history. Thirty-nine patients (58.2%) had positive PCR work colleagues, twenty patients (29.85%) had contact with positive family members, five patients (7.46%) had contact from school and three patients (4.48%) had no known contact history.

### Data regarding the systemic history

History recorded regarding systemic symptoms of COVID-19 was noted to document the manifestation of COVID-19 and its association

with ocular symptoms. Twenty-two (47.76%) patients had a fever, 18 (26.87%) had a cough, 16 (23.88%) patients had a sore throat, and 11 (16.42%) patients had no systemic symptoms. Information on other systemic illness patients was collected for its association with ocular symptoms. 37 patients (55.22%) had no systemic illness, 15 patients (22.39%) had diabetes mellitus, 11 (16.42%) had hypertension, 3 (4.48%) had cardiovascular disorder and one patient had thyroid disorders.

### Data regarding the ocular history

Fifty-nine of 67 patients had conjunctival congestion suggestive of conjunctivitis. Eight (12%) patients had developed ciliary injection due to keratitis in 7 patients and 1 patient of corneal ulcer. In 861 cases of COVID-19 PCR-positive patients, a total of 67 patients that consulted to ophthalmologist were included in the study with ocular complaints comprising all patients is redness, ocular burning sensation in ten patients, watering eyes in eight patients, and photophobia in eight patients. Sixty out of 67 (89.55 %) patients developed ocular manifestation along with COVID-19-related systemic symptoms while seven (10.45%) patients developed ocular manifestation before any COVID-19-related systemic symptoms. History regarding the risk factors for conjunctivitis including eye protection usage, history of eye disease, and previous ocular surgery was collected. Eighteen (26.87%) patients were using spectacles, four (6%) patients had a history of cataract surgery and the rest patient had no previous history of any eye diseases.



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**Table 1.** Patients’ demographics

Variable	Number	Percentage
Gender		
Male	39	58.21
Female	28	41.79
Contact history		
Working relation	39	58.21
Family Member	20	29.85
School	5	7.46
No contact	3	4.48

**Table 2.** Systemic and ocular manifestation

Variable	Number	Percentage
Systemic symptoms		
Fever	32	47.76
Cough	18	26.87
Sore throat	16	23.88
No symptom	11	16.42
Comorbidities		
No systemic illness	37	55.22
Diabetes mellitus	15	22.39
Hypertension	11	16.42
Cardiovascular	3	4.41
Thyroid disorders	1	1.49
Ocular manifestation		
Hyperemia		
Burning sensation	67	100
Epiphora	10	14.93
Photophobia	8	11.94
	8	11.94
Risk Factors		
No ocular history	35	52.24
Using spectacles	18	26.87
History of cataract surgery	4	5.97



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### DISCUSSION

Zhou's research showed that angiotensin-converting enzyme 2 (ACE2) is the main receptor against the SARS-CoV-2 virus and increased expression of ACE-2 will increase the ability to fight SARS-CoV-2 (Ni, W., Yang, X., Yang, D. *et al*, 2020). ACE2 receptors can be found in tissues such as the lungs, kidneys, nervous system, cardiac, gastrointestinal, hepatic, and endocrine. Research by Collin and Zhou reported the expression of ACE-2 in normal human conjunctiva, adult epithelium, and limbus. Several studies have shown that in the collection tissue, conjunctiva, anterior eye fluid, and human retina, there are ACE2 receptors that will bind to SARS-CoV-2. CoV-2 so that these cells become infected (Zhou L *et al*, 2020).

The second mechanism is the migration of the virus in the ocular fluid through the nasolacrimal duct during the presence of an upper respiratory tract infection. Currently, there is no further explanation regarding this mechanism (Durak, S. *et al*, 2021). The translucent appearance of the conjunctiva allows for immediate visualization of changes in the circulation of the conjunctival microvasculature consisting of extensive branching of superficial and deep arterial systems and corresponding drainage pathways, and the translucent appearance of the conjunctiva allows for immediate visualization of changes in the circulation. Conjunctival hyperemia is caused by a pathological vasodilatory response of the microvasculature in response to inflammation due to a myriad of infectious and non-infectious etiologies (RB Singh., *et al* 2021). SARS-CoV-2 can be detected on the ocular surface through a conjunctival swab by Reverse Transcriptase-Polymerase Chain Reaction although only in a small percentage (Danthuluri V, Grant MB, 2020). The low percentage of virus found in

conjunctival swabs due to the low expression of ACE2 in the conjunctival tissue layer and comparison with the amount of ACE2 expressed in heart and lung tissue (Li G *et al*, 2020). In this study, a Reverse Transcriptase-Polymerase Chain Reaction from a conjunctival swab was not performed due to limited hospital facilities.

Studies suggest that there are many differences between men and women in the immune response to SARS-CoV-19, affecting more men than women (Conti P, Younes A (2020). However, this article did not compare the differences between women and men. We were unable to determine any relationship between the presence of conjunctivitis and clinical, radiological, or laboratory severity in our sample of 67 cases.

The absence of ocular manifestations does not rule out the presence of the virus in ocular fluid, and conversely, the presence of ocular manifestations does not exclude the virus's absence in ocular fluid. The risk of transmission of SARS-CoV-2 through tears may be low but this does not rule out that the varying results may be due to the virus residing in the conjunctiva or tears that can only survive for a very short period, but it can also be due to differences in the volume of fluid obtained, fluid collection technique, or sampling time. During the sampling, the virus entered the nasolacrimal duct for this reason, data on the sensitivity and specificity of SARS-CoV-2 RT-PCR are not yet available (Güemes-Villahoz N *et al*, 2021).

Posterior segment abnormalities such as optic neuritis, disk edema, vascular tortuosity, acute macular neuro retinopathy (AMN), vasculitis retinal occlusion (RVO), retinal artery occlusions, intraretinal hemorrhages, cotton wool spots, uveitis, and endogenous endophthalmitis have all been reported in COVID-19 patients. This study only performed





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anterior segment examination because the highly transmittable of COVID-19 disease limits the posterior segment examination.

### CONCLUSION

Ocular signs and symptoms often appear as early manifestations in COVID-19 patients without other systemic manifestations. Although the percentage of ocular manifestation is low, precautions and early treatments are needed, because this ocular manifestation can develop into severe and life-threatening conditions. Conjunctivitis manifesting as conjunctival injection is common and is one of the major ocular manifestations in COVID-19-positive patients. Early identification of conjunctivitis can be detected by ophthalmologists so the transmission can be reduced.

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