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ORIGINAL ARTICLE



# Outcomes of the Ophthalmic Examinations in Patients Infected by SARS-CoV-2

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**ABSTRACT**

**Purpose**: To evaluate ophthalmic examination results which were performed with slit-lamp biomicroscope, in patients with laboratory-confirmed SARS-CoV-2 infection.

**Methods**: In the present study, 50 patients with laboratory-confirmed SARS-CoV-2 infection, were enrolled. Ophthalmic examination with slit-lamp biomicroscopy was performed and the results were evaluated.

**Results**: The mean age of 50 patients (24 females, 26 males) included in this study, was 58,26 ± 18,91 years. In nine patients, bilateral acute follicular conjunctivitis was present. In two patients, acute anterior uveitis was seen. Optic disc and macula were normal in all patients. Preauricular lymphadenopathy (LAP) was found in 6 (12%) patients. Of these six patients, five had follicular conjunctivitis, and one had anterior uveitis.

**Conclusion**: Acute follicular conjunctivitis with preauricular LAP and anterior uveitis were detected and no fundus pathologies were found in detailed ophthalmic examination in patients with laboratory-confirmed SARS-CoV-2 virus infection.

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**KEYWORDS**
SARS-CoV-2; ocular manifestation; ocular disease

Coronaviruses are enveloped positive-sense RNA viruses that primarily target the human respiratory system. Previous outbreaks of coronaviruses (CoVs) include the severe acute respiratory syndrome (SARS-CoV) and the Middle East respiratory syndrome (MERS-CoV).[1] In December 2019, new cases of a "pneumonia with unknown etiology" were reported in Wuhan, China, and the pathogen was identified as a novel coronavirus (2019-nCoV /COVID-19) in January 2020.[2] This new coronavirus was then named SARS-CoV-2 because of its close similarity to SARS-CoV-1.[3]

The most common symptoms of patients infected by SARS-CoV-2 are fever, cough, and fatigue.[4] However, clinical features revealed by a chest computer tomography (CT) scan present as pneumonia, and the disease can also be manifested by extreme symptoms that may lead to death such as acute respiratory distress syndrome, acute cardiac injury, and incidence of ground-glass opacities.[5]

Ophthalmic manifestations are apparently uncommon in patients infected by SARS-CoV-2. Zhang et al. reported two cases of conjunctivitis in a clinical study of 72 patients with laboratory-confirmed SARS-CoV-2 infections.[6] On the other hand, Wu et al. found that 31.6% of patients had conjunctivitis in a clinical study of 38 patients infected by SARS-CoV-2.[7]

Chen et al. reported a case of bilateral acute follicular conjunctivitis. The diagnosis was made by using a slit-lamp biomicroscope.[8] To the best of our knowledge, no clinical study has revealed the results of a biomicroscopic examination of patients with a laboratory-confirmed SARS-CoV-2 infection.

The aim of the present study was to evaluate the results of ophthalmic examinations performed with a slit-lamp biomicroscope in patients with laboratory-confirmed SARS-CoV-2 infections.

## Materials and Methods

This cross-sectional observational study was conducted at Sakarya University Education and Research Hospital in April 2020. All 50 patients included in the study consisted of hospitalized patients. These patients were evaluated with a positive real-time reverse transcription-polymerase chain reaction (rRT-PCR) test using nasopharyngeal and oropharyngeal swabs, and they were hospitalized. Low-dose chest CT was performed as necessary. Systemic diseases such as essential hypertension, diabetes mellitus, chronic obstructive pulmonary disease, and asthma were investigated and noted. Laboratory findings (e.g., of D-dimers, C-reactive proteins, urea, creatinine, ferritin, lactic dehydrogenase, lymphocytes, and neutrophils) reported in patient records were noted, as were body temperature and the details of patient treatment.

Ophthalmic examination was performed by slit-lamp biomicroscopy. One ophthalmologist performed all ophthalmic examinations in a well-ventilated room while wearing full personal protective equipment, including goggles, an N95 respirator, and disposable surgical gloves. The eyelids, bulbar conjunctiva and palpebral conjunctiva, cornea, and anterior segment were examined. The anterior chamber was assessed in a dimmed room. The optic disc and macula were evaluated with slit-lamp biomicroscopy by using a + 90 diopter. Preauricular LAP was also investigated and noted.

The systemic disease was classified as mild, moderate, or severe according to the severity of the disease. The clinical appearance of all patients included in the study was mild or moderate. Patients with respiratory failure who needed artificial ventilation or followed in intensive care units were excluded from the study.

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### Statistical Analysis

Statistical analysis was performed using SPSS statistical software (IBM SPSS Statistics, Version 23.0, Armonk, NY: IBM Corp.). Descriptive analyses were performed to provide information on the general characteristics of the study population. The Kolmogorov–Smirnov test was used to determine whether the distribution of the numerical variables was normal. The numeric variables were presented as mean ± standard deviation. A $p$-value <0.05 was considered significant.

### Ethical Approval

Prior approval was received from the Institutional Review Board (IRB number: 71522473/050.01.04/159) and written informed consent was obtained from each subject. The study was performed in adherence to the Declaration of Helsinki.

## Results

This prospective study was conducted at Sakarya University Education and Research Hospital in April 2020. The mean age of the 50 patients (24 females, 26 males) included in this study was 58.26 ± 18.91 years. Demographic characteristics, systemic diseases, mean body temperature, and oxygen saturation levels of the patients are shown in Table 1.

Low-dose chest CT was performed on 44 patients (88%). All patients were given oral hydroxychloroquine sulfate (200 mg/day), and 39 patients (78%) were given oral azithromycin (500 mg/day). Nine patients (18%) and eight patients (16%) were given oral oseltamivir phosphate (75 mg/day) and Favipiravir (1200 mg/day), respectively.

Table 2 reports the laboratory findings for the patients.

Ophthalmic examination was performed within 2 weeks after the SARS-CoV virus infection had been confirmed (4.84 ± 3.29 days of hospitalization). In nine patients, follicles were seen in the lower palpebral conjunctiva, and the diagnosis of bilateral acute follicular conjunctivitis was made. In two patients, there were inflammatory cells in the anterior chamber, and the diagnosis of anterior uveitis was made. Optic disc and macula were normal in all patients. Preauricular LAP was found in six patients (12%). Five of these six patients had follicular conjunctivitis and one had anterior uveitis. Ophthalmological symptoms appeared on the 4.74 ± 3.56 (range1-7 days) day of the clinical presentation. Table 3 reports the ocular diseases found upon ophthalmic examination. The complaints of the patients were as follows: tearing (n = 9, 18%), eye itching (n = 8, 16%), photophobia (n = 4, 8%), burning sensation (n = 5, 10%), blurred vision (n = 2, 4%). In addition, patients indicated that none of the patients had ocular symptoms prior to systemic symptoms due to coronavirus disease. Symptomatic treatment was applied to patients with ocular findings (such as preservative-free artificial tears, cold compress, and lubricating ophthalmic ointment). All patients with ocular findings were followed by us until their ocular findings were resolved. The ophthalmologic findings of all patients improved within 3 weeks with symptomatic treatment without any complications.

**Table 1.** Demographic and clinical characteristics of patients.

| Variables | N % |
|---|---|
| Gender (F/M) | 24/26 (52,0%/48,0%) |
| Mean Age (mean±SD, years) | 58.26 ± 18.91 |
| Presence of HT (n, %) | 7(14,0%) |
| Presence of COPD (n, %) | 2(4,0%) |
| Presence of Asthma (n, %) | 2(4,0%) |
| Presence of DM (n, %) | 1(2,0%) |
| The mean body temperature (mean±SD, °C) | 36.93 ± 0.70°C |
| $O_2$ saturation level (mean±SD) | 96.02 ± 2.78 |

F/M: Female/Male, SD: standard deviation, HT: hypertension, COPD: chronic obstructive pulmonary disease, DM: diabetes mellitus.

**Table 2.** Laboratory findings of patients with SARS-CoV-2 infection.

| Variables | N | Mean | Std. Deviation | Minimum | Maximum |
|---|---|---|---|---|---|
| Albumin (g/L) | 44 | 32.803 | 6.8630 | 0.6 | 43.8 |
| Alanine aminotransferase (U/L) | 50 | 40.10 | 33.877 | 8 | 143 |
| Aspartate aminotransferase (U/L) | 50 | 40.91 | 29.105 | 10 | 167 |
| CRP (mg/L) | 50 | 41.3086 | 48.95292 | 3.02 | 199.00 |
| D-dimer (µg/L) | 49 | 1925.69 | 5057.799 | 3 | 33900 |
| Serum ferritin (ng/mL) | 42 | 440.1919 | 514.44173 | 9.08 | 2545.06 |
| Hemoglobin (g/L) | 50 | 12.0122 | 2.20309 | 0.09 | 16.10 |
| Creatinine (mg/dL) | 50 | 1.0174 | 1.46897 | 0.48 | 11.00 |
| Lactate dehydrogenase (U/L) | 47 | 318.87 | 126.163 | 25 | 577 |
| Lymphocyte count ($10^9$/L) | 50 | 2.4752 | 5.79867 | 0.58 | 42.30 |
| MPV(fL) | 49 | 9.1966 | 1.95850 | 6.34 | 17.70 |
| Neutrophil count ($10^9$/L) | 50 | 4.4518 | 2.45037 | 1.14 | 13.20 |
| Platelet count ($10^9$/L) | 50 | 254.33 | 115.042 | 16 | 625 |
| Urea (mg/dL) | 50 | 38.98 | 18.639 | 6 | 90 |
| White blood cell count ($10^9$/L) | 50 | 6.4654 | 2.39262 | 2.51 | 13.00 |

CRP: C reactive protein, MPV: mean platelet volume.

**Table 3.** Ophthalmic examination findings of patients.

| Variables | N | % |
|---|---|---|
| Follicular conjunctivitis | 9 | 18,0 |
| Blepharoconjunctivitis | 4 | 8,0 |
| Blepharitis | 4 | 8,0 |
| Papillary conjunctivitis | 3 | 7,5 |
| Anterior uveitis | 2 | 4,0 |
| Presence of cataract | 2 | 4,0 |
| Presence of pterygium | 1 | 2,0 |

## Discussion

In the present study, acute follicular conjunctivitis was observed in 18% of patients with laboratory-confirmed SARS-CoV infections. Wu et al. observed 12 patients with conjunctivitis in 38 patients with clinically confirmed SARS-CoV-2 infections.[7] Zhang et al. observed only two patients with conjunctivitis in 72 patients with laboratory-confirmed SARS-CoV-2 infections.[6] The type of conjunctivitis suffered by these patients was not mentioned in these studies. Chen et al. reported the case of a patient with bilateral acute follicular conjunctivitis.[8] Follicular conjunctivitis may be seen in a variety of conditions, including inflammation caused by pathogens such as viruses, atypical

bacteria, and toxins.[9] Ophthalmologists have been familiar with this type of bilateral acute follicular conjunctivitis and with outbreaks due to adenoviruses.[10,11] Coronaviruses have also been known to manifest in ocular tissues.[12] In their 2005 study, Vabret et al. found that 17% (n = 3) of HCoV-NL63 patients (n = 18) had developed conjunctivitis.[13] The new coronavirus, SARS-CoV-2, seems to cause acute follicular conjunctivitis, but not at a frequent rate.

Preauricular LAP was seen in six patients, five of whom had follicular conjunctivitis as well. Preauricular LAP is a common finding in viral follicular conjunctivitis.[10,14] Thus, in the follicular conjunctivitis associated with the SARS-CoV-2 virus, preauricular LAP may accompany other ocular findings. On the other hand, the presence of preauricular LAP in viral anterior uveitis is uncommon. In one patient, mild anterior uveitis and preauricular LAP were present together, but this may be only a coincidence. The herpes virus, the West Nile virus, the Ebola virus, retroviruses, and the togavirus are among the viruses that may cause different types of uveitis.[15] Anterior uveitis associated with coronavirus in humans was not reported previously. This item should be furtherly searched in the patients with laboratory-confirmed SARS-CoV-2 virus infection to detect traces of uveitis.

We think that the reason for the differences in ophthalmic findings in the studies may be due to the difference in systemic disease severity of the patient groups included in the study. In fact, our study did not only consist of patients with ophthalmological complaints.

In many other studies, anterior segment examination was performed with a binocular ophthalmoscope. However, in our study, unlike other studies, slit-lamp biomicroscope was used. We think that we can get better information with this examination method.

In the present study, concomitant ophthalmic diseases including mainly blepharoconjunctivitis and papillary conjunctivitis were present in patients with laboratory-confirmed SARS-CoV-2 virus infection. We have already known that ocular diseases frequently cause and increase the rate of hand-ocular surface contact time. Several studies suggested a transmission route from conjunctiva and revealed the importance of prevention by washing hands, not touching to eyes, and wearing protective goggles in hospitals.[6–8,16] Thus, increasing eye-hand contact time might increase the risk of virus transmission.

The major limitation of the present study was performing ophthalmic examinations in different days of hospitalization and in different days of treatment. This might be altered by the results. The absence of tears or conjunctival swabs and the inclusion of a small number of patients are other limitations of our study. On the other hand, a detailed ophthalmic examination of the 50 patients with laboratory-confirmed SARS-CoV-2 virus infection gave us more information about the ocular manifestations of this infection.

## Conclusion

In conclusion, follicular conjunctivitis with preauricular LAP and anterior uveitis were detected and no fundus pathologies were found in detailed ophthalmic examination in patients with laboratory-confirmed SARS-CoV-2 virus infection. After the outbreak ends, enhanced studies should be performed to understand the effects of this infection on ocular structures.

## Declaration of interest

The authors report no conflict of interest.

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