

# Concomitant Ocular Diseases in Patients with SARS-CoV-2 Infection

## SARS-CoV-2 Enfeksiyonlu Hastalarda Eşlik Eden Oküler Hastalıklar

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### Abstract

Objective	To investigate the presence of chronic ocular diseases in patients who had a real-time reverse transcription-polymerase chain reaction (rRT-PCR) test of oropharyngeal/nasopharyngeal swabs for SARS-CoV-2 virus.
Materials and Methods	A retrospective chart review was conducted to determine all hospitalized patients who had a positive rRT-PCR test for SARS-CoV-2 virus. From these patients, who applied to eye polyclinics in the last one year were included and the diagnosis was investigated.
Results	This study investigated 1120 patients with a positive rRT-PCR test. Of these patients, 178 (15.8%) had applied to eye clinics previously. The most common diseases were refractive errors, dry eye syndrome, blepharconjunctivitis, and allergic conjunctivitis.
Conclusion	The rate of concomitant ocular diseases in patients with confirmed SARS-CoV-2 was 15.8%. Avoiding touching the face and eyes and hand hygiene were the main prevention ways from SARS-CoV-2 infection. Concomitant ocular diseases might increase the risk of contact transmission routes.
Keywords	Eye disease; SARS-CoV-2; COVID-19

### Öz

Amaç	Nazofaringeal ve orofaringeal sürüntülerde SARS-CoV-2 virüsü için gerçek zamanlı ters transkripsiyon-polimeraz zincir reaksiyonu (rRT-PCR) testi pozitif olan hastalarda oküler hastalıkların varlığını araştırmak.
Gereç ve Yöntemler	SARS-CoV-2 virüsü açısından rRT-PCR testi pozitif olan hastanede yatan hastaların dosyaları geriye dönük tarandı. Bu hastalardan son bir yıl içinde göz polikliniğine başvuran hastalar çalışmaya dahil edildi ve almış oldukları tanımlar kayıt edildi.
Bulgular	Bu çalışmada rRT-PCR testi pozitif olan 1120 hasta incelendi. Bu hastaların 178'i (% 15,8) daha önce göz kliniklerine başvurmuştu. En sık görülen hastalıklar kırma kusurları, kuru göz sendromu, blefarokonjunktivit ve alerjik konjunktivit idi.
Sonuç	SARS-CoV-2 varlığı doğrulanmış hastalarda eşlik eden oküler hastalık oranı % 15.8 idi. Kronik göz hastalıklarının, el-yüz teması nedeniyle ile SARS-CoV-2 enfeksiyonunun bulaştırıcılığı artırabileceğini düşünüyoruz.
Anahtar Kelimeler	Göz hastalıkları; SARS-CoV-2; COVID-19

## INTRODUCTION

Coronaviruses (CoV) are RNA viruses that can cause a variety of diseases in humans. In humans, the diseases caused by CoV range from mild cold to fatal lower respiratory tract infections.<sup>1</sup> In late 2019, the pathogen of new pneumonia cases reported from China was determined to be a new coronavirus (2019-nCoV-COVID-19), and the virus spread to the whole world within months, causing a massive epidemic.<sup>2</sup> This new coronavirus was then named Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) because of its close similarity to SARS-CoV-1.<sup>2</sup>

Human-to-human transmission of SARS-CoV-2 is usually via respiratory droplets. In addition, transmission may occur through hand-mouth, hand-nose or hand-eye contact.<sup>3,4</sup> The mucosa of the conjunctiva is linked to the upper respiratory tract, and one study reported that conjunctiva may be easily involved in SARS-CoV-2 infection and may act as a route of transmission.<sup>5</sup> Additionally, the angiotensin-converting enzyme 2 (ACE2) receptors found in the epithelium of the cornea and conjunctiva play a major role in the entry of viruses into host cell membranes.<sup>6,7</sup>

Relationships between SARS-CoV-2 infection and common systemic diseases, such as diabetes mellitus (DM) and essential hypertension (HT), have been established.<sup>8</sup> Based on the hypothesis that chronic eye diseases may increase the rate of getting the disease by increasing hand eye contact, this study was designed. The aim of the current study was to investigate the presence of chronic ocular diseases in patients who had a positive real-time reverse transcription-polymerase chain reaction (rRT-PCR) test of nasopharyngeal and oropharyngeal swabs.

## MATERIALS and METHODS

The current study was designed as a retrospective descriptive study. Prior approval was received from the Institutional Review Board Sakarya University Faculty of Medicine Ethics Committee, 07/04/2020, IRB number:050.01.04/158), and written informed consent was

obtained from each subject. The study was performed in adherence to the Declaration of Helsinki.

A retrospective chart review was conducted to determine all hospitalized patients who had a positive rRT-PCR test of nasopharyngeal and oropharyngeal swabs between March and April 2020. Patients who applied to eye polyclinics in the last one year were included in this study. The application information and diagnosis of the patients was obtained from the hospital information management system. Additionally, the presence of chronic systemic diseases, such as HT, DM, chronic obstructive pulmonary disease (COPD), and asthma, were noted. The results of blood tests and low-dose chest computerized tomography (CT) were also evaluated.

Patients with chronic ocular disease such as dry eye syndrome, refractive errors, blepharconjunctivitis, glaucoma, and age-related macular degeneration were included in the study. Patients admitted for acute eye diseases, ocular trauma and eye surgery were not included in the study. 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 evaluate whether the distribution of the numerical variables was normal. The numeric variables were presented as mean  $\pm$  standard deviation. An independent t-test or Mann-Whitney U test was used to compare parameters. The categorical variables were compared with a Chi-square test. A p-value  $< 0.05$  was considered significant.

## RESULTS

This study included 1120 patients with a positive rRT-PCR test. Of these patients, 178 (15.80%; 90 female, 88 male) had applied to eye clinics previously. The mean age of the patients was  $55.82 \pm 16.22$  years. The chest CT results of 143 (80.30%) patients revealed findings compatible with SARS-CoV-2 infection. Table 1 shows the additional

chronic systemic diseases of these patients, and Table 2 summarizes the laboratory findings of the patients. The results of the blood tests were not different between the female and male patients, except those of blood urea tests. Table 3 shows the distribution of ocular diseases in patients. The most common diseases were refractive errors, dry eye syndrome, blepharoconjunctivitis, and allergic conjunctivitis. Allergic conjunctivitis was more common in females ( $p < 0.05$ ), while blepharoconjunctivitis was more common in males ( $p < 0.05$ ).

**Table 1:** Chronic systemic diseases of patients with COVID-19

Variable	N:178
Sex (M/F, %)	88/90 (49,40/50,60)
The mean age (mean±SD)	55,82± 16,22 years
Presence of HT (n, %)	30 (16,90)
Presence of DM (n, %)	8 (4,50)
Presence of asthma (n, %)	8 (4,50)
Presence of COPD (n, %)	4 (2,20)

M/F: male/female, SD: standard deviation HT: hypertension DM: diabetes mellitus COPD: chronic obstructive pulmonary disease

**Table 2:** Laboratory findings of patients with COVID-19

Variable	N	Mean	SD	Median	Min	Max
D-dimer (µg/L)	173	1769.11	5155.59	443.00	0.00	39300.00
CRP (mg/L)	155	53.63	68.83	36.40	1.00	570.00
Albumin (g/L)	136	34.54	6.17	34.10	19.50	47.90
Urea (mg/dL)	170	42.32	39.29	36.00	9.00	282.00
Creatinine (mg/dL)	172	0.99	1.11	0.76	0.39	9.19
Serum ferritin (ng/mL)	170	547.85	1742.91	275.63	5.22	20426.04
Lactate dehydrogenase (U/L)	168	296.11	170.68	286.00	138.00	1767.00
Lymphocyte count (109/L)	173	1.43	0.70	1.20	0.20	3.80
Neutrophil count (109/L)	150	4.49	3.60	3.70	0.89	20.70

SD: standard deviation, Min: minimum, Max: maximum

**Table 3:** Distribution of chronic ocular diseases in patients with COVID-19

Variable	N (%)
Refractive errors	104 (58,40)
Dry Eye Syndrome	64 (36,00)
Blepharoconjunctivitis	50 (28,00)
Allergic Conjunctivitis	26 (14,60)
Cataract	15 (8,40)
Glaucoma	9 (5,10)
Diabetic retinopathy	7 (3,90)
Age related macular degeneration	5 (2,80)
Pterygium	4 (2,20)

## DISCUSSION

As mentioned previously, one of the main transmission routes of the SARS-CoV-2 virus is contact transmission: touching a contaminated surface or object and subsequently touching the mouth, nose, or eyes.<sup>4,9</sup> Thus, regular handwashing with soap or disinfection with hand sanitizer containing at least 60% alcohol (if soap and water are not available); avoidance of contact with infected people by maintaining an appropriate distance as much as possible; and refraining from touching the eyes, nose, and mouth with unwashed hands have been advised to all people for prevention.<sup>10</sup>

Ocular diseases frequently cause and increase the rate of hand-ocular surface contact time. The main symptoms of dry eye syndrome are itching, burning, stinging, and a sandy sensation.<sup>10,11</sup> Additionally, similar symptoms have been observed in patients with allergic conjunctivitis and blepharoconjunctivitis.<sup>12,13</sup> Furthermore, wearing glasses might prevent respiratory droplet transmission, but might also cause more contact with the face. There is a study showing that regular use of glasses due to refractive errors can reduce the likelihood of getting COVID-19 disease. Zeng et al.'s study found that in patients with COVID-19 were less likely to wear glasses than the general population, suggesting that daily use of glasses is associated with less susceptibility to COVID-19 infection.<sup>14</sup> In the current study, the most common ocular diseases were refractive errors, dry eye syndrome, blepharoconjunctivitis, and allergic conjunctivitis. These diseases (especially ocular surface diseases) can cause severe hand-eye contact, thereby increasing the risk of transmission.

The current study aimed to identify concomitant ocular diseases in patients infected by the SARS-CoV-2 virus. Chen et al. retrospectively investigated 534 patients infected by the SARS-CoV-2 virus and found conjunctivitis, dry eye syndrome, keratitis, cataract, and diabetic retinopathy history in 85 patients; the rate of concomitant ocular disease was found to be 15.9%.<sup>15</sup> This rate was remarkably

similar to the result found by the current study, which was 15.8%.

Other studies have investigated presumed ocular manifestations of SARS-CoV-2 virus infection.<sup>15-18</sup> For example, out of 72 patients with confirmed SARS-CoV-2 infection, Sun et al. found two patients with conjunctivitis and only one of them had a positive rRT-PCR test of a conjunctival swab.<sup>19</sup> Additionally, Chen et al. found a man with follicular conjunctivitis whose rRT-PCR test from conjunctival swab was positive.<sup>20</sup> Wu et al. found that a total of 12 of 38 patients (31.6%; 95% CI, 17.5-48.7) had ocular manifestations consistent with conjunctivitis, including conjunctival hyperemia, chemosis, epiphora, or increased secretion.<sup>21</sup> In the study conducted by Boz et al., anterior uveitis and acute follicular conjunctivitis were detected in patients with SARS-CoV-2 virus infection, but no fundus pathology was observed.<sup>22</sup> The study of Bozkurt et al. showed that COVID-19 patients may have pathological conjunctival changes without clinically significant ocular symptoms.<sup>23</sup> All these studies suggested a transmission route from conjunctiva and revealed the importance of prevention by washing hands, not touching eyes, and wearing protective goggles in hospitals.

## CONCLUSIONS

In conclusion, the rate of previous ocular diseases in patients with a laboratory-confirmed SARS-CoV-2 was found to be 15.8%. The most common ocular disorders were refractive errors, dry eye syndrome, blepharoconjunctivitis, and allergic conjunctivitis. Further studies with large samples should be performed to extend our information about ocular transmission routes of this highly contagious disease.

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