Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), responsible for the current pandemic of corona virus disease 2019 (COVID-19), is highly contagious and has posed a tremendous threat to global public health. Recent studies have reported that this novel coronavirus strain may produce conjunctival findings and can be detected in tears and conjunctival secretions. An implication is that there may be a potential hazard to healthcare workers, especially the ophthalmologists, who perform examination in close proximity to COVID-19 patients and may come in contact with tears or conjunctival secretions. In December 2019, Wuhan, China, became the epicenter of the COVID-19 pandemic, and we undertook a cross-sectional study to characterize ocular symptoms, examine conjunctival swabs for presence of SARS-CoV-2 RNA, and determine whether a correlation existed between ocular findings and duration of disease.

From January 17 through February 16, 2020, a total of 121 patients who had been managed in the Renmin Hospital of Wuhan University were recruited. Based on the standard of the National Health Commission of China, all patients were confirmed COVID-19 cases with at least 1 positive result for SARS-CoV-2 from respiratory specimens, such as nasopharyngeal swabs or sputum, or other clinical specimens, such as blood or stool, using real-time reverse-transcriptase polymerase chain reaction (RT-PCR) or genetic sequencing, or positive results for specific antibody through the serologic test. Clinical disease was classified as mild, moderate, severe, or critical based on disease severity. The study was approved by the ethics committees of Renmin Hospital of Wuhan University and was conducted with strict adherence to the tenets of the Declaration of Helsinki.

Written informed consent was obtained from all patients before the study. Relevant clinical information and any ocular symptoms that developed either at onset or during the later course of the disease were obtained through the review of medical records and implementation of the external eye examination with a penlight. We collected the conjunctival and nasopharyngeal swabs from all patients on the same day. The conjunctival samples were obtained from one of the affected eyes of patients with ocular symptoms or randomly from 1 eye of patients without ocular symptoms. All the sampling operations were carried out by 2 experienced physicians (Y.Z. and C.D.). The presence of SARS-CoV-2 RNA was detected by real-time RT-PCR assay in a clinical diagnostic laboratory with the kits and protocols recommended by the Chinese Center for Disease Control and Prevention.

We used the paired chi-square test (McNemar-Bowker test) to compare the proportion with positive results for SARS-CoV-2 RNA between nasopharyngeal and conjunctival swab samples. The Fisher exact test was used to analyze the statistical correlation between the proportion of patients with ocular symptoms and conjunctival SARS-CoV-2 detection. For the ordinal categorical variable, the Spearman rank correlation analysis was performed to assess the statistical correlation between the proportion of patients with ocular findings and the duration of disease. All statistical analyses were performed using the statistical software package IBM SPSS Statistics version 26.0 (IBM, Chicago, IL).

Of the 121 patients with confirmed COVID-19, 63 patients (52.1%) had mild or moderate disease and 58 patients (47.9%) had severe or critical disease. The median age was 48 years (range, 22–89 years) and the male-to-female ratio was 0.78 (53:68). The mean ± standard deviation of the duration of disease was 15.0 ± 8.8 days. Eight patients (6.6%) showed ocular symptoms; only 1 of them showed positive results for SARS-CoV-2 in the conjunctiva. The ocular symptoms and abbreviated findings included itching (5 [62.5%]), redness (3 [37.5%]), tearing (3 [37.5%]), discharge (2 [25%]), and foreign body sensation (2 [25%]). The 1 patient with ocular symptoms and positive SARS-CoV-2 conjunctival swab results was classified as a severe or critical case. Two patients without ocular symptoms showed positive results for conjunctival SARS-CoV-2, with one of them classified as a severe or critical case and another classified as a mild or moderate case. Of 8 patients with ocular symptoms, 7 were severe or critical cases and 1 was a mild or moderate case. For the correlation analyses of these ocular findings and the duration of disease, we additionally found that the proportion of patients with ocular symptoms was not correlated statistically with the duration of disease (Table 1; Spearman rank correlation analysis: correlation coefficient, 0.111; \( P = 0.22 \)) and that the proportion with positive results for conjunctival SARS-CoV-2 was not correlated statistically with the duration of disease, either (Table 1; Spearman rank correlation analysis: correlation coefficient, 0.074; \( P = 0.42 \)).

The proportion with positive results for conjunctival SARS-CoV-2 detection was 2.5% (3/121), which was significantly different from the nasopharyngeal SARS-CoV-2 detection rate (Table S1, available at www.aaojournal.org; positive proportion, 2.5% vs. 70.2%; McNemar-Bowker test: chi-square value, 85.571; \( P < 0.001 \)). Of 3 patients who showed positive results for conjunctival SARS-CoV-2, 2 were severe or critical cases and 1 was a mild or moderate case. The finding of ocular symptoms was not associated significantly with the results of conjunctival SARS-CoV-2 detection (Table S2, available at www.aaojournal.org; odds ratios, 2.548 [95% confidence interval, 0.268–24.192]; \( P = 0.39 \), Fisher exact test).

Our study has several limitations. First, because of the risk to healthcare workers and the acuity of the condition of patients, we were unable to perform biomicroscopic slit-lamp examination. Second, the conjunctival swabs were collected at only 1 time point. Recent data obtained from an animal study suggest that the presence of the virus may be transient in conjunctiva after ocular conjunctival inoculation. Therefore, the single time point for conjunctival sampling and a wide range of time from diagnosis to sampling may have reduced recovery rates. This may be compounded by the possible false-negative rate of real-time RT-PCR assays. Finally, the study is limited by the small number of patients.
In conclusion, this study characterizes the ocular symptoms in COVID-19 patients, reports the proportion of samples with positive conjunctival and nasopharyngeal RT-PCR results from patients with COVID-19, and incorporates the duration of disease into the analysis. A minority of the 121 patients showed ocular symptoms and findings, which when present were mild. Three of 121 patients showed positive RT-PCR results from conjunctival swabs. The appearance of symptoms and penlight findings or the results of positive conjunctival swab analysis were not correlated significantly with the duration of disease. One patient showed both symptoms and positive conjunctival swab results and was classified as a severe or critical case; 2 patients showed no symptoms but revealed positive swab results, with one classified as a severe or critical case and another was classified as a mild or moderate case. The proportion with positive results for SARS-CoV-2 RNA was significantly different between the conjunctival and nasopharyngeal specimens. However, this study is limited by its small number of patients. The potential for conjunctival transmission of SARS-CoV-2 is worth further exploration. Recognizing the risk for viral exposure, all physicians and ophthalmologists should adopt proper precautions to reduce the risk for disease transmission while caring for patients.

**References**