Ocular manifestations and clinical characteristics of 535 cases of COVID-19 in Wuhan, China: a cross-sectional study

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ABSTRACT.

Purpose: To investigate the ocular manifestations and clinical characteristics of COVID-19 patients caused by SARS-CoV-2 in Wuhan, China.

Methods: A total of 535 COVID-19 patients were recruited at Mobile Cabin Hospital and Tongji Hospital. Information on demographic characteristics, exposure history, ocular symptoms, eye drop medication, eye protections, chronic eye diseases, systemic concomitant symptoms, radiologic findings and SARS-CoV-2 detection in nasopharyngeal swabs by real-time PCR was collected from questionnaires and electronic medical records.

Results: Of 535 patients, 27 patients (5.0%) presented with conjunctival congestion and 4 patients had conjunctival congestion as the initial symptom. The average duration of conjunctival congestion was 5.9 ± 4.5 days (mean [SD]). The other ocular symptoms, including increased conjunctival secretion, ocular pain, photophobia, dry eye and tearing, were also found in patients with conjunctival congestion. Notably, hand–eye contact was independently correlated with conjunctival congestion in COVID-19 patients. We also found that some COVID-19 patients had chronic eye diseases, including conjunctivitis (33, 6.2%), xerophthalmia (24, 4.5%) and keratitis (14, 2.6%). Similar to the published studies, the most common clinical symptoms were fever, cough and fatigue. A total of 343 patients (64.1%) had positive SARS-CoV-2 detection in nasopharyngeal swabs.

Conclusions: Conjunctival congestion is one of the COVID-19-related ocular symptoms, which could occur as the initial symptoms. Frequent hand–eye contact may be the risk factor for conjunctival congestion in COVID-19 patients. Screening of patients with conjunctival congestion by ophthalmologists is advocated during the outbreak of COVID-19. It is essential to provide eye-care equipment and strengthen education on eye protection.

Key words: conjunctival congestion – COVID-19 – hand-eye contact – ocular manifestations – SARS-CoV-2

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Introduction

The ongoing outbreak of the novel coronavirus disease (COVID-19) has been declared by WHO as a global public health emergency. COVID-19 was first reported in Wuhan, China, in December 2019, followed by an outbreak across Hubei Province, other parts of China and now all over the world, particularly in America, Spain, Italy and Germany (Huang et al. 2020). This serious infectious disease is caused by a novel enveloped RNA betacoronavirus, named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (Lu et al. 2020a,b). A study in the New England Journal of Medicine by Zhong Nanshan and colleagues reported nine cases with conjunctival congestion among the 1,099 cases enrolled (Guan et al., 2020). Besides, a recent paper found that 31.6% COVID-19 patients had ocular manifestations consistent with conjunctivitis, including conjunctivitis (33, 6.2%), xerophthalmia (24, 4.5%) and keratitis (14, 2.6%). Similar to the published studies, the most common clinical symptoms were fever, cough and fatigue. A total of 343 patients (64.1%) had positive SARS-CoV-2 detection in nasopharyngeal swabs.

Key words: conjunctival congestion – COVID-19 – hand-eye contact – ocular manifestations – SARS-CoV-2
angiotensin-converting enzyme 2 (ACE2), similar to SARS-CoV (Wan et al., 2020; Zhou et al., 2020). Moreover, the expression and activity of ACE2 can be detected in the ocular surface, including the cornea and conjunctiva, which provides transocular entry potential for SARS-CoV-2 (Sun et al., 2004).

Several urgent questions need to be addressed, including (1) What are the detailed profiles of COVID-19-related ocular symptoms and diseases? (2) What are the clinical characteristics of COVID-19 patients with conjunctival congestion? and (3) Can COVID-19 spread through the ocular route or present as the primary infected site? To answer these questions, it is essential to perform ocular screening among patients with COVID-19. To our knowledge, comprehensive ophthalmological data on COVID-19 are still missing. Hence, the present cross-sectional study was designed to describe the ophthalmic characteristics of COVID-19 patients in Wuhan, aiming to get a complete ocular screening of COVID-19, which may provide clinical clues for the diagnosis and treatment of the disease and a theoretical basis for appropriate protection guidelines in the population.

Materials and Methods

Study population

The study was conducted in accordance with the Declaration of Helsinki. It has been approved by the ethics committee of Tongji Hospital and the China Ethics Committee for Registering Clinical Trials (ChiCTR2000030489). Informed consent was obtained from the patients involved.

A total of 3149 patients were recruited from 1 February to 1 March 2020, at Mobile Cabin Hospital of Optical Valley and Tongji Hospital of Huazhong University of Science and Technology in Wuhan, China. The exclusion criteria were as follows: (1) current hospitalized patients; (2) severe COVID-19 patients; (3) patients without smartphone; (4) unable to contact by telephone; and (5) refused questionnaire. After evaluation with the exclusion criteria, a total of 535 patients were finally valid for the study (flow chart presented in Fig. 1). Diagnosis and classifications of COVID-19 were made according to the novel coronavirus infection pneumonia diagnosis and treatment guideline, 7th edition (National Health Commission of the People’s Republic of China).

Data collection

Demographic, epidemiological, clinical, laboratory and radiologic data were obtained from patients’ electronic medical records and an electronic questionnaire completed by patients on a smartphone. Data about ocular manifestation, the use of eye drops and eye protection were obtained by ophthalmologists via telephone. If data were missing from the questionnaire or clarification was needed, we communicated directly with the patient by telephone after obtaining informed consent. Two researchers independently reviewed the data collection forms to double-check the data collected.

For the reason of safety and disease control, the slit lamp examinations or other ophthalmic examinations cannot be realized. For the patients reporting conjunctival congestion or conjunctivitis, we further did the basic ophthalmic examinations with flashlight or send them a representative picture of conjunctival congestion to confirm their symptoms.

Nucleic acid detection of SARS-CoV-2 in nasopharyngeal swabs

Nasopharyngeal swabs were collected from all patients by a trained health-care worker using protective equipment. The swab samples were maintained in a viral-transport medium stored between 2°C and 8°C. All samples were analysed by conventional qualitative reverse transcription polymerase chain reaction (RT-PCR). RNA was extracted from the clinical samples using a viral RNA kit. A 25 μl reaction containing 5 μl of RNA, 12.5 μl of 2 × reaction buffer provided with the one-step RT-PCR system with Platinum Taq Polymerase (Invitrogen, Darmstadt, Germany; containing 0.4 mM of each deoxyribonucleotide triphosphates (dNTP) and 3.2 mM magnesium sulphate), 1 μl of reverse transcriptase/Taq mixture from the kit, 0.4 μl of a 50 mM magnesium sulphate solution (Invitrogen), and 1 μg of nonacetylated bovine serum albumin. The SARS-CoV-2 specific primers are as follows: forward primer 5′-ACTTCTTTTTTCCTGCTTTCGTG-3′; reverse primer 5′-GCAGCTACGCACACAATC-3′; and the probe 5′-CY5-CTAGTTACACTAGCCATCC TTACTGC-3′-BHQ1. (Huangetal.2020) These primers were used to detect the...
Table 1. Demographics and baseline characteristics of COVID-19 patients by conjunctival congestion.

| Demographics and baseline characteristics | Without conjunctival congestion (N = 508) | With conjunctival congestion (N = 27) | p value |
|-------------------------------------------|------------------------------------------|--------------------------------------|---------|
| Median age (IQR) – years                  | 44.0 (34.0-54.2)                         | 44.0 (28.5-53.5)                     | 0.529   |
| Age group – no. (%)                       |                                          |                                      |         |
| <15 year                                  | 0                                        | 0                                    | 0.211   |
| 15-44 year                                | 259 (51.0%)                              | 15 (55.6%)                          |         |
| 45-64 year                                | 235 (46.3%)                              | 10 (37.0%)                          |         |
| ≥65 year                                  | 14 (2.8%)                                | 2 (7.4%)                            |         |
| Female sex – no. (%)                      | 255 (50.2%)                              | 12 (44.4%)                          | 0.56    |
| Occupation – no. (%)                      |                                          |                                      |         |
| Employee                                  | 207 (45.8%)                              | 5 (20.0%)                           |         |
| Self-employed                             | 85 (18.8%)                               | 5 (20.0%)                           |         |
| Unemployed                                | 79 (17.5%)                               | 4 (16.0%)                           |         |
| Retired                                   | 36 (8.0%)                                | 3 (12.0%)                           |         |
| Agricultural worker                       | 22 (4.9%)                                | 3 (12.0%)                           |         |
| Student                                   | 9 (2.0%)                                 | 3 (12.0%)                           |         |
| Medical staff                             | 14 (3.1%)                                | 2 (8.0%)                            |         |
| Smoking history – no. (%)                |                                          |                                      | 0.464   |
| Never smoked                              | 456 (89.8%)                              | 23 (85.2%)                          |         |
| Former smoker                             | 29 (5.7%)                                | 2 (7.4%)                            |         |
| Current smoker                            | 23 (4.5%)                                | 2 (7.4%)                            |         |
| Exposure history within past 14 days – no. (%) |                                      |                                      |         |
| Huanan Seafood Wholesale Market           | 5 (1.0%)                                 | 0                                    | 1.000   |
| Contact with person with fever            | 149 (29.3%)                              | 10 (37.0%)                          | 0.393   |
| Contact with COVID-19 patient in family or community | 193 (38.0%)                              | 10 (37.0%)                          | 0.921   |
| Chronic medical illness – no. (%)         |                                          |                                      |         |
| Hypertension                              | 65 (12.8%)                               | 5 (18.5%)                           | 0.390   |
| Diabetes mellitus                         | 37 (7.3%)                                | 1 (3.7%)                            | 0.712   |
| Hyperlipidaemia                           | 6 (1.2%)                                 | 0                                    | 1.000   |
| Cardiovascular and cerebrovascular diseases | 18 (3.5%)                                 | 0                                    | 1.000   |
| Respiratory system disease                | 36 (7.1%)                                | 1 (3.7%)                            | 1.000   |
| Haematological system disease             | 3 (0.6%)                                 | 0                                    | 1.000   |
| Chronic kidney disease                    | 3 (0.6%)                                 | 0                                    | 1.000   |
| Chronic liver disease                     | 25 (4.9%)                                | 0                                    | 1.000   |
| Autoimmune disease                        | 8 (1.6%)                                 | 2 (7.4%)                            | 0.086   |

Data are presented as median (IQR) or number (percentage). p values are calculated from Kruskal–Wallis test, chi-square test or Fisher’s exact test.

* p value < 0.05.

Clinical characteristics of COVID-19 patients by conjunctival congestion

The clinical characteristics, including the common symptoms of COVID-19, the radiologic findings of chest CT and the PCR results of SARS-CoV-2 detection, in nasopharyngeal swabs are summarized in Table 2.

The clinical symptoms of the patients in two groups were similar, but the percentages of involvement were various. The most common symptoms were fever (66.7% and 60.8% in patients with or without conjunctival congestion, respectively), cough (74.1% and 64.8%, respectively) and fatigue (51.9% and 29.3%, respectively) or with a confirmed COVID-19 case in the family or community (37.0% and 38.0%, respectively). The top three ranked chronic illnesses were same in patients with or without conjunctival congestion, including hypertension (18.5% and 12.8%, respectively), diabetes mellitus (3.7% and 7.3%, respectively) and respiratory system disease (3.7% and 7.1%, respectively).

Results

Demographics and baseline characteristics of COVID-19 patients by conjunctival congestion

A total of 535 COVID-19 patients (27 with conjunctival congestion) were enrolled in the study. The demographic data, exposure history and past medical history are summarized in Table 1.

The median age of patients with or without conjunctival congestion was 44 years. The majority (55.6% and 51.0%, respectively) were aged 15–44 years. There was a similar proportion of men and women (15/12 and 253/255, respectively) in the two groups. Nearly half (45.8%) of the patients without conjunctival congestion employed, and 14 (3.1%) infected cases were medical staff; 3 (12.0%) patients with conjunctival congestion were agricultural workers, and 2 (8.0%) patients were medical staff. Among all the subjects with or without conjunctival congestion, most had a contact history with a person with a fever (37.0% and 29.3%, respectively) or with a confirmed COVID-19 case in the family or community (37.0% and 38.0%, respectively). The top three ranked chronic illnesses were same in patients with or without conjunctival congestion, including hypertension (18.5% and 12.8%, respectively), diabetes mellitus (3.7% and 7.3%, respectively) and respiratory system disease (3.7% and 7.1%, respectively).

Statistical analysis

Continuous variables were expressed as medians (interquartile range, IQR) and compared with the Kruskal–Wallis test. Categorical variables were summarized as counts (percentages) and compared by chi-square test or Fisher’s exact test.

Univariate and multivariate regression analysis were used to evaluate correlations between ocular protections and conjunctival congestion. No imputation was made for missing data. All the analyses were performed using Empower (R) (www.empowerstats.com, X&Y Solutions, Inc. Boston, MA) and R (http://www.R-project.org).

The presence of SARS-CoV-2 RNA. All oligonucleotides were synthesized and provided by Tib-Molbiol (Berlin, Germany). The RT-PCR condition was developed by the Clinical Laboratory of Tongji Hospital. Thermal cycling was performed at 55°C for 10 min for reverse transcription, followed by 95°C for 3 min and then 45 cycles of 95°C for 15 s and 58°C for 30 s.
### Table 2. Clinical characteristics of COVID-19 patients by conjunctival congestion.

| Clinical characteristics | Without conjunctival congestion (N = 508) | With conjunctival congestion (N = 27) | p value |
|--------------------------|------------------------------------------|--------------------------------------|---------|
| Symptoms – no. (%)       |                                          |                                      |         |
| Fever                    | 309 (60.8%)                              | 18 (66.7%)                           | 0.544   |
| Highest temperature     |                                          |                                      | 0.582   |
| <37.3°C                  | 199 (39.2%)                              | 9 (33.3%)                            |         |
| 37.3–38°C                | 93 (18.3%)                               | 7 (25.9%)                            |         |
| 38.1–39.0°C              | 170 (33.5%)                              | 10 (37.0%)                           |         |
| >39.0°C                  | 46 (9.1%)                                | 1 (3.7%)                             |         |
| Cough                    | 329 (64.8%)                              | 20 (74.1%)                           | 0.322   |
| Sore throat              | 103 (20.3%)                              | 6 (22.2%)                            | 0.807   |
| Fatigue                  | 196 (38.6%)                              | 14 (51.9%)                           | 0.169   |
| Poor appetite            | 139 (27.4%)                              | 7 (25.9%)                            | 0.870   |
| Chest stuffiness         | 169 (33.3%)                              | 9 (33.3%)                            | 0.994   |
| Shortness of breath      | 84 (16.5%)                               | 4 (14.8%)                            | 1.000   |
| Dyspnoea                 | 113 (22.2%)                              | 7 (25.9%)                            | 0.655   |
| Nasal discharge          | 22 (4.3%)                                | 3 (11.1%)                            | 0.125   |
| Nasal congestion         | 24 (4.7%)                                | 3 (11.1%)                            | 0.149   |
| Headache                 | 115 (22.6%)                              | 6 (22.2%)                            | 0.960   |
| Myalgia or arthralgia    | 147 (28.9%)                              | 8 (29.6%)                            | 0.938   |
| Diarrhoea                | 160 (31.5%)                              | 8 (29.6%)                            | 0.839   |
| Abdominal pain           | 50 (9.8%)                                | 3 (11.1%)                            | 0.742   |
| Radiologic findings – no./total no. (%)  |                                          |                                      |         |
| Chest CT                 |                                          |                                      | 0.059   |
| Single lung              | 90/463 (19.4%)                           | 4/26 (15.4%)                         |         |
| Bilateral lungs          | 354/463 (76.5%)                          | 18/26 (69.2%)                        |         |
| Normal                   | 19/463 (4.1%)                            | 4/26 (15.4%)                         |         |
| Laboratory findings – no. (%) |                                          |                                      | 0.807   |
| SARS-CoV-2 in throat swab specimens by RT-PCR |                                          |                                      |         |
| Positive                 | 325 (64.9%)                              | 18 (66.7%)                           |         |
| Probable positive        | 27 (5.3%)                                | 2 (7.4%)                             |         |
| Negative                 | 156 (30.7%)                              | 7 (25.9%)                            |         |

Data are presented as median (IQR) or number (percentage). P values are calculated from Kruskal–Wallis test, chi-square test or Fisher’s exact test.

### Multivariate regression analysis

Multivariate regression analysis between ocular protections and conjunctival congestion was performed in Table 4. Model I adjusted for age, gender and smoking history. Model II adjusted for the former factors, highest temperature and SARS-CoV-2 detection.

On univariate analysis, the frequency of hand-eye contact was associated with conjunctival congestion. After adjusting for other clinical factors in multivariate regression analysis, the frequency of hand-eye contact was still correlated with conjunctival congestion in model II. The regression coefficient was 4.01 (95% CI, 1.11–14.55, p = 0.035). No significant relation was found between wearing glasses or goggles, time of reading and conjunctival congestion.

### Ocular profiles and clinical characteristics of patients with conjunctival congestion

The ocular symptoms, eye drop medications, eye protections, history of eye disease and clinical characteristics of all 27 patients with conjunctival congestion are summarized in Table 5. The duration of conjunctival congestion, onset date of clinical symptoms and days after clinical symptoms occurring conjunctival congestion are summarized in Fig. 2.

Eight patients had conjunctival congestion and increased conjunctival secretion (cases 4, 6, 8, 12, 13, 14, 19 and 26). Five patients had tearing (cases 2, 4, 6, 11 and 16). Five patients also had ocular pain (cases 1, 7, 10, 21 and 27), and five patients had foreign body sensation in the eyes (cases 4, 7, 17, 21 and 26). Nineteen patients ever touched their eyes with their hands, and 13 (cases 2, 3, 4, 6, 8, 9, 10, 11, 18, 22, 23, 24 and 26) of them did not wash their hands before touching their eyes. Of the patients with conjunctival congestion, most had bilateral lung involvement indicated by chest CT (18/26, 69.2%) and positive PCR results in SARS-CoV-2 detection (18, 66.7%).

The duration of conjunctival congestion ranged from 2 to 24 days. Conjunctival congestion appeared mostly after the first clinical symptoms.
of COVID-19. Four patients (cases 14, 17, 21 and 25) had conjunctival congestion as an initial symptom. Seven patients (cases 5, 7, 11, 16, 18, 22 and 23) developed conjunctival congestion within three days after the beginning of clinical symptoms.

**Discussion**

To date, the epidemiologic data on the incidence of conjunctivitis in COVID-19 patients range from 0.8% to 7.9% (Guan et al., 2020; Wu et al. 2020; Xia et al., 2020; Zhang et al., 2020) However, the precise incidence of ocular manifestations relative to COVID-19 is unclear. In our present study, we found that (1) of a total of 535 COVID-19 patients identified, 27 patients (5.0%) presented with conjunctival congestion; (2) the accompanied ocular symptoms were different between the two groups with or without conjunctival congestion, and dry eye (37.0%), conjunctival secretion (29.6%), tearing (22.2%), ocular pain (18.5%) ranked in the top four in patients with conjunctival congestion group; and 3) simultaneously, we also found the occurrence of conjunctival congestion in COVID-19 patients correlated with a higher frequency of hand–eye contact (22.2% vs. 7.9%).

Most recently, Wu et al. (2020) found that one-third of patients with COVID-19 had ocular abnormalities, consistent with conjunctivitis, including conjunctival hyperaemia or increased secretions. However, these epidemiologic investigations did not fully observe other ocular manifestations besides conjunctival congestion. The present epidemiologic study summarized more manifestations present on the ocular surface mainly in the mild cases. We enrolled 535 patients and similarly found that COVID-19 patients exhibit ocular manifestations including conjunctival congestion (27), secretion (52), foreign body sensation (63), blurred vision (68), dry eye (112), itching (53), photophobia (16) and tearing (55). The demographics and baseline characteristics of COVID-19 patients with or without conjunctival congestion have no significant difference. The incidence of conjunctival congestion in our study is 5.0%, which is lower than Wu’s report (3/38, 7.9%) (Wu et al. 2020) but higher than that in Zhong’s large sample report (9/1099, 0.8%) (Guan et al., 2020) and Xia’s study (1/30, 3.3%) (Xia et al., 2020). Wu found that conjunctival congestion occurred in patients with more severe COVID-19. Zhong and colleagues extracted data from 552 hospitals in 30 provinces, autonomous regions and municipalities in China, while 21 common-type and nine severe-type COVID-19 patients were observed by Xia in Zhejiang Province. However, the COVID-19 patients in our study mainly came from Tongji Hospital (271) or Mobile Cabin Hospital (264) in Wuhan, and they were mostly common-type. Therefore, the clinical type and region may be the causes of the various incidence of conjunctival congestion in COVID-19 patients.

Given that SARS-CoV-2 nucleic acid was not detected in patients’ conjunctival swab sample, we did not diagnosis them with conjunctivitis directly. However, these 27 patients did not report any other chronic eye diseases nor any symptoms associated with intraocular diseases (such as iritis, choroiditis and retinal disease), which suggests that the possibility of endophthalmitis is very small, and conjunctivitis may be the primary cause of the conjunctival congestion. Moreover, conjunctival congestion and positive RT-PCR in pharyngeal swabs were found at the same time in four COVID-19 patients (cases 11, 20, 23 and 24) who reported no...
chronic eye diseases. Our previous study found a rare case of nosocomial SARS-CoV-2 infection initiated with conjunctivitis in a nurse, and both the conjunctival and nasopharyngeal swabs tested for SARS-CoV-2 were positive. (Sun et al., 2020) However, the aim of this epidemiological study is to investigate the ocular manifestations of COVID-19 patients, and most of them were no longer exhibit conjunctival congestion when they performed investigation, which contribute to the conjunctival swab test data missing. Our study also found that the average duration of conjunctival congestion was 5.9 ± 4.5 days (mean [SD]), ranging from two to twenty-four days. Four patients diagnosed with COVID-19 patients had an initial symptom of conjunctival congestion, which reminds us that ocular manifestations occur early in the course of COVID-19. Therefore, healthcare workers should pay attention to patients' ocular symptoms and manifestations in the early stage of disease and should perform a conjunctival swab test for SARS-CoV-2 in patients with conjunctival congestion.

**Table 4.** Correlations between ocular protections and conjunctival congestion in COVID-19 patients by multivariate regression analysis.

|                | Unadjusted | Model I | Model II |  *p* value |
|----------------|------------|---------|----------|------------|
|                |            |         |          |            |
| Wearing glass or goggle | No | 1.00 | 1.00 | 1.00 |
|                | Yes | 1.29 (0.57, 2.94) | 0.546 | 1.31 (0.52, 3.28) | 0.565 | 1.24 (0.49, 3.17) | 0.648 |
| Hand-eye contact | Never | 1.00 | 1.00 | 1.00 |
|                | Seldom | 1.16 (0.47, 2.85) | 0.745 | 0.99 (0.37, 2.69) | 0.989 | 0.92 (0.33, 2.59) | 0.871 |
|                | Often | 3.66 (1.20, 11.11) | 0.022* | 3.88 (1.12, 3.39) | 0.032* | 4.01 (1.11, 14.55) | 0.035* |
| Total time of short-distance reading | <2 hr | 1.00 | 1.00 | 1.00 |
|                | 2-4 hr | 1.04 (0.34, 3.19) | 0.951 | 1.29 (0.36, 4.65) | 0.696 | 1.29 (0.35, 4.76) | 0.698 |
|                | 4-8 hr | 0.67 (0.23, 1.98) | 0.473 | 0.62 (0.17, 2.19) | 0.454 | 0.59 (0.16, 2.13) | 0.417 |
|                | 8-12 hr | 0.76 (0.23, 2.48) | 0.653 | 0.54 (0.13, 2.30) | 0.404 | 0.59 (0.14, 2.58) | 0.483 |
|                | >12 hr | 0.77 (0.15, 3.84) | 0.747 | 0.54 (0.08, 3.51) | 0.519 | 0.46 (0.07, 3.17) | 0.434 |

Data are presented as β (95% CI) p value.
* p value < 0.05. Model I adjust for age, gender, smoking history and occupation. Model II adjust for the former factors, highest temperature and SARS-CoV-2 detection.

**Table 5.** Detailed information about the ocular profiles and clinical characteristics of patients with conjunctival congestion.

| Case | Gender | Age (years) | Ocular symptoms | Eye drops | Glass or goggle | Hand-eye contact | Wash hands before hand-eye contact | Reading | Chronic eye diseases | Clinical characteristics |
|------|--------|-------------|----------------|-----------|----------------|-----------------|-----------------------------|---------|---------------------|------------------------|
| 1    | Male   | 18          | CC, OP, P       | No        | Yes            | Seldom          | >12h                        | No      | No                  | Temp (°C) Chest CT PCR |
| 2    | Male   | 44          | CC, DE, L, T    | No        | No             | Never           | 8-12h                       | No      | No                  | 36.5 Single lung +     |
| 3    | Male   | 25          | CC, BV, DE      | No        | No             | Often           | >12h                        | No      | No                  | 36.7 Normal +          |
| 4    | Female| 30          | CC, CS, FBS, P, BV, DE | No | No | Seldom | No | 4-8h | No | 37.7 Bilateral lungs +/- |
| 5    | Female| 47          | CC              | No        | Yes            | Seldom          | Yes 4-8h                    | No      | No                  | 36.4 Conjunctivitis +   |
| 6    | Female| 33          | CC, CS, DE, T   | Tobramycin | Yes           | No               | 4-8h                        | No      | No                  | 38.5 Bilateral lungs -  |
| 7    | Male   | 18          | CC, OP, FBS, DE | Yes       | No             | Yes             | 8-12h                       | No      | No                  | 36.6 Unclear -          |
| 8    | Male   | 18          | CC, CS          | No        | Yes            | Often           | No 8-12h                    | No      | No                  | 36.8 Normal +          |
| 9    | Male   | 44          | CC, DE          | Ofloxacin | No             | Seldom          | 4-8h                        | No      | No                  | 36.5 Bilateral lungs +  |
| 10   | Female| 27          | CC, OP          | Artificial tears | Yes | Seldom | No | 4-8h | No | 37.8 Xerophthalmia Normal + |
| 11   | Female| 28          | CC, T           | Ganciclovir | Yes | Seldom | No | 2-4h | No | 38.2 Bilateral lungs + |
| 12   | Female| 64          | CC, CS, BV, DE  | No        | No             | Often           | Yes 2-4h                    | No | No                  | 37.5 Bilateral lungs -  |
| 13   | Male   | 56          | CC, CS          | No        | No             | Never           | >2h                         | No      | No                  | 39.0 Bilateral lungs +  |
| 14   | Female| 61          | CC, DC, DE      | No        | No             | Never           | <2h                         | No      | No                  | 38.5 Single lung -      |
| 15   | Male   | 42          | CC              | No        | No             | Often           | Yes 2-4h                    | No      | No                  | 38.6 Bilateral lungs +  |
| 16   | Female| 40          | CC, T           | No        | No             | Never           | 2-4h                        | No      | No                  | 37.7 Bilateral lungs -  |
| 17   | Male   | 65          | CC, FBS         | No        | No             | Never           | 4-8h                        | No      | No                  | 39.0 Bilateral lungs +  |
| 18   | Male   | 45          | CC              | No        | Yes            | Seldom          | No <2h                      | No      | No                  | 39.4 Bilateral lungs +  |
| 19   | Male   | 62          | CC, CS, DE      | Ofloxacin | No             | Seldom          | Yes <2h                     | No      | No                  | 36.8 Bilateral lungs -  |
| 20   | Female| 58          | CC              | Ofloxacin Ganciclovir | No | Never | <2h | No | 39.0 Single lung - |
| 21   | Female| 43          | CC, OP, FBS     | No        | No             | Never           | <2h                         | No      | No                  | 37.0 Bilateral lungs +/- |
| 22   | Male   | 65          | CC, I           | No        | Yes            | Seldom          | No 8-12h                    | No      | No                  | 37.5 Bilateral lungs +  |
| 23   | Male   | 50          | CC, I           | Ofloxacin | No             | Seldom          | No 2-4h                     | No      | No                  | 39.0 Bilateral lungs +  |
| 24   | Female| 51          | CC, I           | No        | No             | Seldom          | No 2-4h                     | No      | No                  | 38.5 Bilateral lungs +  |
| 25   | Male   | 28          | CC              | No        | No             | Never           | 4-8h                        | No      | No                  | 37.5 Bilateral lungs +  |
| 26   | Male   | 29          | CC, CS, FBS, DE, I | Ofloxacin | No          | Often           | 8-12h                       | No      | No                  | 36.5 Conjunctivitis Normal + |
| 27   | Female| 51          | CC, OP, P       | No        | No             | Never           | <2h                         | No      | No                  | 36.5 Bilateral lungs +  |

CC, conjunctival congestion; CS, conjunctival secretion; OP, ocular pain; FBS, foreign body sensation; P, photophobia; BV, blurred vision; DE, dry eye; T, tearing; and I, itching.
+/, positive; +/-, probable positive; and –, negative.
SARS-CoV-2 is thought to be transmitted from person to person mainly through respiratory droplets or close contact (Xu et al. 2020). The ocular surface is exposed to the outside environment, which may become a potential gateway for pathogens such as viruses to invade the human body (Belser et al. 2013; Stiles 2014).
Moreover, eye rubbing is another high risk factor for virus transmission, which has been confirmed in adenovirus-induced conjunctivitis. (Artieda et al. 2010) Simultaneously, we found that a total of 332 COVID-19 patients had a history of hand-eye contact, including 286 cases who reported seldom hand-eye contact and 46 who reported frequent hand-eye contact. Among the 27 cases with conjunctival congestion, 19 (70.4%) had a history of hand-eye contact, 6 (22.2%) with frequent contact. The results of multivariate regression analysis also showed that the high-frequency hand-eye contact correlated with conjunctival congestion, suggesting that hand-eye contact is possibly a risk factor for conjunctival congestion in COVID-19 patients.

The present study also found that the incidence of dry eye, blurred vision and foreign body sensation was the top three ocular symptoms in all patients (20.9%, 12.7% and 11.8%), which could be due to the fact that COVID-19 patients are more likely to have a lot of time to use electronic products. Our results showed that 321 of 535 COVID-19 patients spent more than four hours per day on short-distance reading and 43 of them even spent exceeded 12 hours per day on reading. Because of this, healthcare workers should propose patients reading scientifically and reducing short-distance reading time.

Consistent with previous studies, SARS-CoV-2-infected patients developed respiratory disorders with initial symptoms of fever, cough, chest stuffiness and fatigue, which quickly progress to pneumonia and even shortness of breath (Chen et al. 2020a,b; Huang et al. 2020; Zhu et al. 2020). However, extra-pulmonary manifestations were also observed in a number of patients at the onset of the illness, including headache, myalgia or arthralgia, and diarrhoea, and some even presented with asymptomatic infection (Chen et al. 2020a,b; Rothe et al. 2020). We also found that most of the enrolled COVID-19 patients had bilateral lung accumulation (372/489), and the SARS-CoV-2 RT-PCR test was positive at least once in 343 patients. However, no significant difference was observed between the COVID-19 patients with or without conjunctival congestion.

The present study has some limitations. First, the sample size was relatively small and the covered population excluded severe cases, since only patients with mild symptoms could complete our electronic questionnaire or telephone follow-up. Second, most of the ocular manifestations were self-reported retrospectively by the questionnaire owing to a physical examination by slit lam is not feasible, and conjunctival swab test for SARS-CoV-2 was not performed in early stage. However, a representative picture of conjunctival congestion was send to patients for reference, which made the conjunctival congestion data reasonable. To date, this is the most comprehensive survey with the largest sample related to the eyes. Fourth, no normal population was observed in our study; therefore, a normal control group should be included for comparison in future studies.

**Conclusions**

In conclusion, the significance of understanding the ocular manifestations of our present study lies in (1) helping to deepen the understanding of COVID-19-related eye diseases; identify ocular symptoms, manifestations and clinical outcomes; and enrich the symptom spectrum of COVID-19; (2) observing the difference between the COVID-19 patients with or without conjunctival congestion; and (3) providing a clue that hand–eye contact correlated with conjunctival congestion in COVID-19 patients. Our findings may provide useful information for the diagnosis and treatment of COVID-19. Simultaneously, it also provides clues for patients with ocular symptoms and manifestations in the early stage of disease should perform a conjunctival swab test for SARS-CoV-2 in patients with conjunctival congestion.

**Acknowledgments**

We are grateful to the medical staffs at Mobile Cabin Hospital of Optical Valley and Tongji Hospital for their assistance. This work was supported by the National Natural Science Foundation of China (81974136 and 81900859) and Huazhong University of Science and Technology (2020kyXGY068). Hong Zhang and Xufang Sun designed and co-ordinated the study. Liwen Chen, Chaohua Deng, Xuhui Chen, Huimin Yu, Yuanjun Qin and Ke Xiao collected the data. Liwen Chen performed and analysed the data. Liwen Chen, Bo Chen and Xian Zhang prepared the figures and tables. Liwen Chen, Chaohua Deng and Xuhui Chen wrote the manuscript. All authors reviewed the results, revised the manuscript and approved it for submission. The authors declare that they have no conflicts of interest with the contents of this article.

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Received on April 15th, 2020.
Accepted on April 21st, 2020.

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Source of funding: This work was supported by the National Natural Science Foundation of China (81974136 and 81900859) and Huazhong University of Science and Technology (2020fyXGHJ068).