Incidence and Clinical Characteristic of Ocular Surface Manifestation: An Evaluation of Conjunctival Swab Results in Corona Virus 2019 (COVID-19) Patients in Jakarta, Indonesia

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Abstract

Objectives: This study aimed to investigate the spectrum of ocular characteristics and viral presence in the conjunctival swab of patients with COVID-19.

Methods: Fifty-three patients were recruited from two COVID-19 referral hospitals in Jakarta (Cipto Mangunkusumo Hospital and Persahabatan Hospital) from July 2020 to March 2021. The inclusion criteria were patients who were suspected of or confirmed cases of COVID-19 with or without ocular symptoms. Demographic data, history of COVID-19 exposure, underlying medical condition, systemic symptoms, ocular symptoms, supporting laboratory results, reverse-transcriptase polymerase chain reaction (RT-PCR) of naso-oropharyngeal (NOP) swab and conjunctival swab were collected.

Results: Fifty-three patients who were suspected, probable or confirmed cases of Covid-19 were included. Forty-six out of 53 patients (86.79%) tested positive for either Covid-19 antibody rapid test or naso-oropharyngeal (NOP) swab. Forty-two patients tested positive for NOP swab. Two out of 42 patients (4.76%) who tested positive for NOP swab were also positive for conjunctival swab.

Conclusions: Establishing the relationship between Covid-19 infection, ocular symptoms, and presence of SARS-CoV-2 virus on the ocular surface proves to be challenging. Ocular symptoms did not warrant a positive conjunctival swab result due to nasolacrimal drainage that quickly clears the virus into the respiratory tract. Most importantly, a patient without ocular symptoms can have detectable presence of SARS-CoV-2 virus on the ocular surface. Hence, tear droplets transmission is possible and preventative measures should be implemented. As ocular involvement is often a systemic response rather than local viral activity, detection of the virus in conjunctival swab is low.

Introduction

Since December 2019 until now, a new disease called Coronavirus disease 2019 (COVID-19) had emerged in Wuhan, China. The disease had quickly spread across the globe and become a pandemic that pose a highly serious threat to millions of people. The etiology of the disease is severe acute respiratory syndrome novel coronavirus 2 (SARS-CoV-2), which causes infection of the respiratory tract that can lead to multiple organ infections and result in death. It has similarities in receptors and other properties with the former member of coronavirus (SARS-CoV-1). Previous studies have found that the SARS-CoV-1 could be detected in the conjunctival tissue, although no studies have established the correlation between SARS-CoV-1 infection and the incidence of conjunctivitis [1–4].

Several studies have tried to explain the correlation between SARS-CoV-2 infection and its ocular manifestation, however many results remained controversial [1–3]. The ocular manifestations reported ranged from simple conjunctivitis with symptoms of red eyes, epiphora, conjunctival secretion, and chemosis to keratoconjunctivitis which impacted vision [4–6]. In addition, ocular manifestations of COVID-19 were reported more in adult patients, while it has not been well documented in pediatric population. Speculation was raised whether the manifestations in children are similar to adults, remembering that

COVID-19 had lower incidence in children with COVID-19 with shorter period of disease, and better clinical outcome [3].

As viral transmission is possible through body fluid and mucous membranes, it was speculated that the conjunctival secretion could be a source of transmission from patients infected with COVID-19 [1, 2, 4, 6, 7]. Therefore, this study also focused on detecting the presence of SARS-CoV-2 in conjunctival secretion through reverse transcriptase-polymerase chain reaction (RT-PCR) procedures. To the best of our knowledge, this is the first Indonesian study which explored the spectrum of ocular manifestations and results of conjunctival swab in COVID-19 patients in two general hospitals in Jakarta, Indonesia.

Methods

Definitions

A suspect case of COVID-19 was defined as patient who has either one of the criteria below: (i) patient with acute respiratory tract infection (ARTI) who has a travel history or stay in a country or region in Indonesia which reported local transmission of the disease within 14 days, (ii) patient with signs and symptoms of ARTI who has a contact with a confirmed or probable case of COVID-19 within 14 days, (iii) patient with severe ARTI/pneumonia who needs to be hospitalized and has no other probable etiologies. A probable case of COVID-19 was defined as suspect case with severe ARTI/ARDS or death with clinical symptoms of COVID-19 and has not been confirmed with RT-PCR examination. A confirmed case of COVID-19 was defined as patient with/without symptoms of COVID-19, who has been confirmed with naso-oropharyngeal (NOP) RT-PCR examination [8].

Study design

This cross-sectional study was conducted in two COVID-19 referral hospitals in Jakarta, that is Cipto Mangunkusumo and Persahabatan Hospital. This study has been approved by the Ethics Committee in both institutions and was conducted in accordance with the Declaration of Helsinki. Informed consent was obtained from all participants. We included patients who were hospitalized in either of these hospitals. The inclusion criteria of this study were children or adult who fulfilled the indicator of suspected cases of COVID-19, patients with positive result of COVID-19 rapid test or naso-oropharyngeal RT-PCR test, with or without ocular symptoms. We excluded patients who were critically ill to have the examination and conjunctival swab performed. Recorded audio informed consent was obtained from patients and/or legal guardians for underaged children. This study has obtained ethical clearance from the ethics committee of the Faculty of Medicine, University of Indonesia (ethical approval number: KET-467/UN2.F1/ETIK/PPM.00.02/2020).

Cases were reported by one ophthalmologist from each hospital delegated for this task. As our study began at the early phase of the pandemic, qualitative antibody testing was the only rapid test available and performed with rapid test kit for Covid-19 IgM/IgG. 10μL of blood collected from finger pin-prick was added to the sample pad, then two drops of sample buffer were added. After a 10-min incubation period,

results were interpreted in which the presence of only the control line was negative, the presence of the control line with IgM and/or IgG line was considered positive. NOP RT-PCR swab test was also performed.

After which, patient history was taken, and conjunctival swab were done simultaneously by the ophthalmologist following appropriate infection control and prevention measures. A single conjunctival swab was collected from both eyes using a sterile dacron flocked swab in the lower eyelid fornix without topical anesthesia. The swab was then broken off and placed into a viral transport media inside the sampling tube and stored in a 4 degrees Celsius environment. RT-PCR test of the conjunctival swab was performed to assess the presence of SARS-CoV-2 RNA in the sample and was processed in clinical microbiology laboratory in both hospitals.

Data collection

We collected information on patients' demographic (age, gender), history of contact, underlying medical condition, systemic condition (COVID-19 symptoms, body temperature), ocular manifestation (ocular symptoms, diagnosis, uncorrected visual acuity), supporting examination result, RT-PCR of NOP swab, and RT-PCR of conjunctival swab through questionnaire-styled history taking, physical examination, and patients' medical records. According to guidelines by the National Institute of Health (NIH), severity of systemic symptoms of our study was classified as mild, moderate, or severe. None of the patients in this study were asymptomatic or critical. Guidelines by the NIH stated that asymptomatic or pre-symptomatic patients were those who tested positive for SARS-CoV-2 but experienced no symptoms of Covid-19. Patients with mild illness showed varying symptoms and signs of Covid 19 but without dyspnea, shortness of breath or abnormal chest imaging. Patients with moderate illness showed signs of lower respiratory infection either by physical examination or imaging, with an oxygen saturation (SpO2) ≥ 94% on room air at sea level. Patients with severe illness have SpO2 < 94% on room air at sea level, a ratio of arterial partial pressure of oxygen to fraction of inspired oxygen (PaO2/FiO2) < 300 mm Hg, a respiratory rate > 30 breaths/min, or lung infiltrates > 50%. Patients who were critical included those with respiratory failure, septic shock, and/or multiple organ dysfunction[(9)].

Statistical analyses

All statistical analyses were performed using SPSS software version 24.0 for Mac (SPSS Inc, Chicago, IL, USA). Categorical data were reported in the form of frequency (percentage). Continuous variables were reported in the form of mean ± SD or median (range). Normality of the data was evaluated with Shapiro-Wilk test. Independent t-test was conducted to evaluate the significant difference between means.

Results

A total of 53 patients who were suspected, probable or confirmed cases of Covid-19 were recruited for this study. About 46 out of 53 patients (86.79%) tested positive for either Covid-19 antibody rapid test or NOP swab, while 4 out of 13 patients with positive antibody rapid test tested negative for both NOP and conjunctival swabs. In 42 patients tested positive for NOP swab. 2 out of 42 patients (4.76%) who tested

positive for NOP swab were also positive for conjunctival swab test. The number of days between NOP and conjunctival swabs ranged from 0 to 7 days with median of 2 days.

About 30 out of 42 patients (71.4%) experienced several systemic symptoms such as anosmia, fever, dyspnea, cough, myalgia, and gastrointestinal symptoms. While 21 out of 42 patients (50%) had systemic comorbidities such as diabetes, hypertension, hyperthyroidism, coronary artery disease, chronic kidney disease, leukemia and systemic lupus erythematosus. About 17 out of 42 patients (40.5%) had ocular complaints such as red eye, epiphora and eye discharge. None of the patients with ocular complaints tested positive in conjunctival swab. The 2 patients who had symptoms of viral conjunctivitis but did not have positive results from conjunctival swab. None of the 2 patients who tested positive in conjunctival swab had ocular symptoms. Clinical characteristics of the patients who tested positive for conjunctival swab and the patients who were diagnosed with Covid-19-related conjunctivitis were summarized in Table 2.

Table 1
Summary of Covid-19 tests result

Type of Test	No. of Patients Tested Positive
Rapid Test Only	4
Rapid Test and NOP RT-PCR	9
NOP RT-PCR Only	31
NOP and Conjunctival RT-PCR Positive	2

Table 2
Clinical characteristics of patients with positive conjunctival RT-PCR results and patients with Covid-19-related conjunctivitis with negative conjunctival RT-PCR results

Patient No.	Age	Sex	Ocular Symptoms	Systemic Severity	NOP Swab	Conjunctival Swab (CS)	Difference between NOP and CS (days)
26	69	M	None	Mild	Positive	Positive	1
28	52	F	None	Mild	Positive	Positive	0
10	55	F	Red eye, itchiness, discharge	Mild	Positive	Negative	2
49	11	M	Red eye	Moderate	Positive	Negative	2

The 42 patients with positive NOP swab ranged from 1 to 69 years old with a mean age of 33.69 ± 22.38 years old. The mean age of the group with positive conjunctival swab was 60.50 ± 12.02 years old, while that of the negative group was 32.35 ± 22.01 years old. However, there was no significant difference in age between the two groups ($p = 0.093$, Table 3). Laboratory results collated which included blood count,

procalcitonin, ureum, creatinine, alanine aminotransferase (ALT), aspartate aminotransferase (AST) as well as C-reactive protein were not significantly different between the two groups as shown in Table 3.

Table 3
Comparison of laboratory results between patients with positive and negative conjunctival swab results

Variable	Positive Conjunctival Swab (n = 40)	Negative Conjunctival Swab (n = 2)	P-value*
Mean age (years)	60.5 ± 12.02	32.35 ± 22.01	0.093
Body temperature (^{o}C)	36.15 ± 0.21	36.65 ± 0.45	0.347
Hemoglobin	13.40 ± 1.27	12.14 ± 2.69	0.656
Platelet count	173.50 ± 21.92	267.10 ± 149.87	0.164
Procalcitonin	0.21 ± 0.11	3.59 ± 11.88	0.468
Urea	37.00 ± 22.63	36.60 ± 40.05	0.790
Creatinin	1.00 ± 0.28	1.39 ± 2.61	0.519
ALT	44.50 ± 30.41	60.15 ± 127.99	0.668
AST	52.00 ± 28.28	50.57 ± 91.53	0.733
CRP	127.05 ± 72.90	57.58 ± 62.43	0.985
*Independent t-test			

Discussion

The mucous membrane of the upper respiratory tract is the main portal entry of SARS-CoV-2. The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection is initiated after type 2 transmembrane protease (TMPRSS2) cleaves the viral spike glycoprotein, which then binds to the angiotensin-converting enzyme 2 (ACE-2) receptor or cluster differentiation 147 (CD 147) of the host cell forming an antigen-receptor complex. Endocytosis of the virus then occurs and cathepsin L (CTSL) cleaves the virus to release viral single stranded RNA into cellular cytosol. Presence of ACE-2 receptors, TMPRSS2 and CTSL in the ocular surface makes it a potential port of entry for SARS-CoV-2[10, 11].

Two patients were positives Covid 19 from conjunctival swab in our study. However, they did not experience any ocular symptoms. Hence, viral entry through the ocular route is a cause of concern as detectable viral presence in the ocular surface is not always symptomatic and eye-hand-eye as well as hand-eye transmission are possible. Although the public has gained awareness in the proper usage of face masks, eye protection such as the use of face shield and goggles is less common. Emergence of variants with higher transmissibility might necessitate further protective measures such as the use of eye protection in conjunction with wearing double masks and also immediate vaccination[10, 12, 13]. Viral entry

into the ocular surface can be caused by direct exposure to droplets, aerosol, contact with contaminated ophthalmic instruments or hand to eye contact after touching a contaminated surface. Indirect entry into the ocular surface can occur through the reflux of NOP secretion into the lacrimal passage which then drains to the ocular surface, or through blood circulation or viraemia that causes entry of the virus into the ocular surface through ocular blood supply.[10, 14]

The possibility of ocular surface acting as port of entry was recently demonstrated by Deng et al whose study showed that conjunctival inoculation of SARS-CoV-2 in rhesus macaques yielded mild interstitial pneumonia and viral load was detected in oropharynx and nasopharynx samples. However, viral load of the conjunctival sample was detected only in the first day after conjunctival inoculation. Intra-tracheal inoculation of SARS-CoV-2 did not yield a detection of viral load in the conjunctival sample[15].

We found 2 cases of patients with positive conjunctival swabs and NOP swabs, 40 patients who tested positive for NOP swabs only and 11 who tested negative for both conjunctival and NOP swabs. The low rate of viral detection in conjunctival samples for our study (2 out of 42 patients with positive NOP samples (4.76%) might be due to several causes. First, majority of the patients in our sample group might be exposed to the virus via the upper respiratory tract pathway instead of the ocular surface. As the virus would descend from the upper to the lower respiratory tract, viral load was therefore not detected in the conjunctival samples. The second probable reason was a fast clearance rate of the virus from the ocular surface due to drainage via the nasolacrimal pathway, therefore SARS-CoV-2 was not detected in the conjunctival samples. This is supported by the study of Deng et al stated that conjunctival viral load was not detected after the first day of inoculation via the conjunctiva of rhesus macaques[15]. Other studies have also found low rates of positive conjunctival swab results ranging from 0 to 11.1% [1, 2, 6, 11, 16, 17].

Two patients (patient no. 10 and 49) were diagnosed with viral keratoconjunctivitis related to SARS-CoV-2 infection. Symptoms included red eye, itchiness, and eye discharge. However, conjunctival samples were negative for SARS-CoV-2. NOP and conjunctival swabs were taken 2 days apart for both patients. The patients were given topical antiviral, topical anti-inflammatory eyedrops as well as artificial tears. Symptoms were relieved and the patients recovered without ocular complications. In contrast, for the 2 patients who tested positive for conjunctival swabs, ocular symptoms were not observed. NOP and conjunctival swabs were taken 0 and 1 day apart. Previous studies also showed low rates of positive conjunctival samples from confirmed COVID-19 cases that ranged between 1.6–7.1%. A low percentage of patients with conjunctivitis who had positive conjunctival swab results was reported[11]. A study by Ranzenigo et al[18] revealed that the presence of ocular symptoms was related to the severity of illness. However, none of the patients in the study with ocular symptoms tested positive for conjunctival swab. These studies along with our results suggested that the occurrence of conjunctivitis is a systemic response rather than local activity of the virus on the ocular surface. However, ocular involvement in Covid-19 patients other than conjunctivitis has been described, including keratitis, uveitis, retinal pathologies, and neuro-ophthalmological involvement.[19] These clinical manifestations often occur in patients who required mechanical ventilation and in patients with more severe illness.[20] As our patients

who had positive conjunctival swab results and mild symptoms of systemic Covid-19, ocular symptoms were not observed. Nevertheless, a link between presence of SARS-CoV-2 in conjunctival sample and ocular symptoms is difficult to establish and elusiveness of the virus on the ocular surface can be caused by nasolacrimal drainage of the virus. Furthermore, ocular involvement is often a result of systemic response, explaining the low positive conjunctival swab rate in Covid-19 patients with ocular involvement.

Laboratory results of patients with positive conjunctival swab results was not significantly different from patients with negative conjunctival swab results as shown in Table 3. A previous study by Atum et al also found no significant difference in laboratory result characteristics between the two groups[(21)]. However, this might be due to the small number of patients who had positive conjunctival swab results and might not be statistically representative of the cohort.

Conclusion

The presence of ocular symptoms might not warrant a positive conjunctival swab result while the presence of SARS-CoV-2 virus on the ocular surface might not cause ocular symptoms. 40.5% of patients with positive NOP swab results had ocular symptoms, 26.19% had a history of ocular disease and 4.76% patients were diagnosed with viral conjunctivitis. The rate of positive conjunctival swab result was 4.76%, the rate of patients who had both conjunctivitis and positive conjunctival swab result was 0%. Nasolacrimal drainage of the virus from the ocular surface might be a reason for the low rate of positive conjunctival swab results in our sample. As ocular symptoms often occur as a systemic response rather than local viral activity, conjunctival swabs were negative for our patients who experienced symptoms of conjunctivitis. More extensive studies need to be carried out to identify the relationship between presence of SARS-CoV-2 in the ocular surface and ocular symptoms of Covid-19 patients.

Abbreviations

Coronavirus disease 2019 (COVID-19), severe acute respiratory syndrome novel coronavirus 2 (SARS-CoV-2), severe acute respiratory syndrome novel coronavirus 1 (SARS-CoV-1), reverse transcriptase-polymerase chain reaction (RT-PCR), naso-oropharyngeal (NOP), National Institute of Health (NIH), alanine aminotransferase (ALT), aspartate aminotransferase (AST), type 2 transmembrane protease (TMPRSS2), angiotensin-converting enzyme 2 (ACE-2) receptor, cluster differentiation 147 (CD 147), cathepsin L (CTSL)

Declarations

Ethics approval and consent to participate: Recorded audio informed consent was obtained from patients and/or legal guardians for underaged children. This study has obtained ethical clearance from the ethics committee of the Faculty of Medicine, University of Indonesia (ethical approval number: KET-467/UN2.F1/ETIK/PPM.00.02/2020).

Consent for publication: Not applicable.

Availability of data and material: The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Authors' contributions: MS analyzed the data and wrote the paper, HD, DF and DAD collected conjunctival swab samples from patients, JDB, DE, AAV, PP, NDP recruited patients for the study, BB and BH analyzed samples from the conjunctival swabs, JC obtained informed consent and clinical data of patients, RSS conceptualized, coordinated and headed the study.

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References

1. Güemes-Villahoz N, Burgos-Blasco B, Arribi-Vilela A, Arriola-Villalobos P, Rico-Luna CM, Cuiña-Sardiña R, et al. Detecting SARS-CoV-2 RNA in conjunctival secretions: Is it a valuable diagnostic method of COVID-19? J Med Virol. 2021;93(1):383–8.
2. Kumar K, Prakash AA, Gangasagara SB, Rathod SBL, Ravi K, Rangaiah A, et al. Presence of viral RNA of SARS-CoV-2 in conjunctival swab specimens of COVID-19 patients. Indian J Ophthalmol. 2020;68(6):1015–7.
3. Valente P, Iarossi G, Federici M, Petroni S, Palma P, Cotugno N, et al. Ocular manifestations and viral shedding in tears of pediatric patients with coronavirus disease 2019: a preliminary report. J aapos. 2020;24(4):212–5.
4. Wu P, Duan F, Luo C, Liu Q, Qu X, Liang L, et al. Characteristics of Ocular Findings of Patients With Coronavirus Disease 2019 (COVID-19) in Hubei Province, China. JAMA Ophthalmol. 2020;138(5):575–8.
5. Cheema M, Aghazadeh H, Nazarali S, Ting A, Hodges J, McFarlane A, et al. Keratoconjunctivitis as the initial medical presentation of the novel coronavirus disease 2019 (COVID-19). Can J Ophthalmol. 2020;55(4):e125-e9.
6. Xia J, Tong J, Liu M, Shen Y, Guo D. Evaluation of coronavirus in tears and conjunctival secretions of patients with SARS-CoV-2 infection. J Med Virol. 2020;92(6):589–94.

7. Zhou Y, Zeng Y, Tong Y, Chen C. Ophthalmologic evidence against the interpersonal transmission of 2019 novel coronavirus through conjunctiva. medRxiv. 2020:2020.02.11.20021956.
8. Indonesia KKR. Pedoman dan Pencegahan Pengendalian COVID-19. 2020.
9. Health NIo. Clinical Spectrum of SARS-CoV-2 Infection 2021 [updated 19 October 2021. Available from: https://www.covid19treatmentguidelines.nih.gov/overview/clinical-spectrum/.
10. Barnett BP, Wahlin K, Krawczyk M, Spencer D, Welsbie D, Afshari N, et al. Potential of Ocular Transmission of SARS-CoV-2: A Review. Vision (Basel). 2020;4(3).
11. Sopp NM, Sharda V. An Eye on COVID-19: A Meta-analysis of Positive Conjunctival Reverse Transcriptase-Polymerase Chain Reaction and SARS-CoV-2 Conjunctivitis Prevalence. Optom Vis Sci. 2021;98(5):429–36.
12. de Freitas Santoro D, de Sousa LB, Câmara NOS, de Freitas D, de Oliveira LA. SARS-COV-2 and Ocular Surface: From Physiology to Pathology, a Route to Understand Transmission and Disease. Front Physiol. 2021;12:612319.
13. Planas D, Veyer D, Baidaliuk A, Staropoli I, Guivel-Benhassine F, Rajah MM, et al. Reduced sensitivity of SARS-CoV-2 variant Delta to antibody neutralization. Nature. 2021.
14. Kharel Sitaula R, Khatri A, Janani MK, Mandage R, Sadhu S, Madhavan HN, et al. Unfolding COVID-19: Lessons-in-Learning in Ophthalmology. Clin Ophthalmol. 2020;14:2807–20.
15. Deng W, Bao L, Gao H, Xiang Z, Qu Y, Song Z, et al. Ocular conjunctival inoculation of SARS-CoV-2 can cause mild COVID-19 in rhesus macaques. Nat Commun. 2020;11(1):4400.
16. Cao K, Kline B, Han Y, Ying GS, Wang NL. Current Evidence of 2019 Novel Coronavirus Disease (COVID-19) Ocular Transmission: A Systematic Review and Meta-Analysis. Biomed Res Int. 2020;2020:7605453.
17. Zhang X, Chen X, Chen L, Deng C, Zou X, Liu W, et al. The evidence of SARS-CoV-2 infection on ocular surface. Ocul Surf. 2020;18(3):360–2.
18. Ranzenigo M, Bruzzesi E, Galli L, Castagna A, Ferrari G. Symptoms and signs of conjunctivitis as predictors of disease course in COVID-19 syndrome. J Ophthalmic Inflamm Infect. 2021;11(1):35.
19. Szczęśniak M, Brydak-Godowska J. SARS-CoV-2 and the Eyes: A Review of the Literature on Transmission, Detection, and Ocular Manifestations. Med Sci Monit. 2021;27:e931863.
20. Ekici Gok Z, Gok A, Acun Delen L, Kasapoglu US, Gurbuz E, Mutlu K. Evaluation of eye care and ocular findings in critically ill COVID-19 patients. Int J Clin Pract. 2021:e14909.
21. Atum M, Boz AAE, Çakır B, Karabay O, Köroğlu M, Öğütlü A, et al. Evaluation of Conjunctival Swab PCR Results in Patients with SARS-CoV-2 Infection. Ocul Immunol Inflamm. 2020;28(5):745–8.