MEDWIN PUBLISHERS
Committed to Create Value for Researchers

Open Access Journal of Ophthalmology
ISSN: 2578-465X

Can the Novel Coronavirus be found in the Ocular Tissues and Secretions? An Opinion

Avinash V Prabhu[1]*, Sayan Mukerjee[2], Gaurav Dubey[3], Anush Nayak[4] and Vibha Kumari[5]

[1]FLAHS, Ramaiah University of Applied Sciences, Bangalore, Karnataka, India

[2]Nandeep School of Optometry, Sangli, Maharashtra, India

[3]Department of Optometry, UP University of Medical Sciences, Saifai, Etawah, India

[4]Department of Optometry, Netra Jyothi Institute of Allied Health Sciences, Udupi, Karnataka, India

[5]Department of Paramedical Sciences, School of Nursing sciences & Allied Health, Jamia Hamdard, New Delhi, India

***Corresponding author:** Avinash V Prabhu, FLAHS, MS Ramaiah University of Applied Sciences Bangalore, India, Email: avinash.prabhu10@gmail.com

Mini Review

Volume 5 Issue 2

Received Date: October 05, 2020

Published Date: October 30, 2020

DOI: 10.23880/oajo-16000204

Abstract

The novel coronavirus outbreak has reached pandemic proportions in a short time, like other respiratory viruses. Respiratory droplets transmit the virus; various body fluids and secretions such as nasopharyngeal swabs, stool, digestive tract, urine, saliva; few anecdotal reports indicate that the virus may be present in ocular secretions and possibilities of transmission by the lacrimal-pump mechanism through tears, thus posing a transmission risk.

An exposed ocular surface acts as a gateway for various respiratory viruses. Looking at the nasolacrimal system anatomical and physiological aspects, it bridges the eye and respiratory tissues. Moreover, it can also share some common viral binding receptors. The eye is less frequently involved in SARS-CoV, and conjunctivitis is the only reported complication so far. The positivity of CoV RNA in conjunctival swabs tested by RT-PCR assay in confirmed SARS-CoV patients is low. The ocular route of coronavirus transmission and its detection in the ocular secretions is still controversial. In this narrative analysis, we reviewed the latest literature and explored an in-depth understanding of the ocular consequences of coronaviruses recorded up to now. The search took place for the corresponding journal through the use of the PubMed, PubMed Central (PMC), Daily situations reports, IPC (Invention Prevention Control) guidelines, WHO (World health organization), and from other Internet Sources. To avoid community transmission risk, the general public must also take precautionary measures in relation to the pandemic COVID-19.

Keywords: Coronavirus; COVID-19; Ocular Manifestation; Severe Acute Respiratory Syndrome; Bronchiolitis

Abbreviations: IPC: Invention Prevention Control; PMC: PubMed Central; WHO: World health organization; HCoV: Human Coronavirus; ACE2: Angiotensin-Converting Enzyme 2.

Introduction

The multi-country outbreak of the novel coronavirus disease is still on its foothold. Originating from Wuhan, Coronaviruses are single-stranded positive-sense RNA viruses. These are the causative organisms for upper respiratory tract infections. Coronaviruses like Human Coronavirus (HCoV)-229E, HCoV-NL63, HCoV-OC43, and HCoV-HKU1 causing mild self-limiting symptoms are known in the records [1,2]. The epidemic is exceptionally infectious and is spread from person to person by respiratory secretions (Droplet from coughing, sneezing, or rhinorrhea) within 1 meter of the infected person [3]. Unexplained

pneumonia characterized by fever, dry cough, exhaustion, and intermittent gastrointestinal symptoms emerged in the Wuhan, Hubei, China market in December 2019 and had a 66% dissemination rate within the working community [4]. It typically affects immune-compromised individuals with systemic morbidities. These viruses are recognized to bezoonotically transmitted and cause secondary transmission from human to human [5-7]. The transmission of SAS-CoV-2 is believed through the infected person's body fluids when the person coughs or sneezes. The respiratory droplets containing the virus are highly contagious. They can eventually infect another person through inhalation, touching surfaces contaminated with the virus, direct contact with the face, mucous membranes of the mouth, and the eyes. The mucous membranes of the mouth, nose, and eyes are common routes of various microbial transmissions. The exposed Ocular surface can also play a significant role in transmission as well as acquiring the virus. The ocular way of coronavirus transmission and its detection in the ocular secretions is still controversial. In this regard, we have reviewed the latest literature and reported the eye effects of coronaviruses.

Methodology

This search for the journal was undertaken through the use of the PubMed, PubMed Central (PMC), Daily situations reports, IPC (Invention Prevention Control) guidelines, WHO (World health organization), and from other Internet Sources.

Evidence of Human Coronavirus (Hcovs)-NL63, SARS-Cov-1 in the Ocular Surface and Secretions

The first study released in March 2004 reported a new strand called HCOV-NL63 in a seven-year-old boy with symptoms of pneumonia, bronchiolitis, and conjunctivitis from nasopharyngeal aspirants [8]. One year later, in the 2005 retrospective report, 18 children tested positive for HCoV-NL63 with upper respiratory tract disease in their nasal swabs, 3(17%) with conjunctivitis [9]. Although they had not collected any ocular swabs. A case series reporting virus detection in conjunctical swabs is recorded from the SARS-CoV in 2003. One female healthcare worker yielded SARS positivity only in tears [10]. In a prospective interventional case series to identify SARS-CoV by RT-PCR in conjunctival scrapings of 17 confirmed patients, none of them was positive for viral RNA [11]. 126 specimens from conjunctiva, throat, and urine were collected between 6 and 8 weeks of illness [12]. Therefore the results are highly inconsistent. To the best of our knowledge to date, there are no reports of conjunctivitis or any other ocular complications reported for SARS-CoV-1 or MERS-CoV in humans.

Evidence of the Novel Coronavirus (SARS-Cov-2) in the Ocular Surface and Secretions Mode of Spread of Covid-19

Since the break-out of SARS-CoV in 2003, SARS-CoV RNA in conjunctival swabs examined by reverse-transcriptase polymerase chain reaction (RT-PCR) assay was positive for 3(37%) of 8 confirmed SARS patients in their early disease process [13].

After this incident, there is an increased awareness of ocular transmission. WHO suggested wearing protective eyewear when examining COVID-19 patients as the exposed ocular surface may be an alternative route for viral transmission? A detailed retrospective analysis was performed in March to identify 1099 laboratory-confirmed COVID-19 cases, conjunctival congestion found in 9(0.8 percent) cases [14]. Conjunctivitis was the first symptom of bilateral source, rubbing, and watering in an anesthesiologist when a patient without safe eyes was examined for Novel Coronavirus Pneumonia with fever and difficult hospitals. These conjunctival swabs were screened to be negative for viral RNA. This study recruited 67 patients of confirmed and suspected NCP patients, only one patient yielded conjunctival swabs positivity, and two were suspiciously positive for viral RNA. Still, none had ocular symptoms, whereas all nasopharyngeal swabs were positive [15]. In the meantime, some of the prospective studies also reported similar kind of results.

Conjunctival squabs were obtained from conjunctival test papers approximately 2 to 3 days after the onset and tested in RT-PCR in a prospective procedure sequence of 30 patients with reported NCP. Twice, one patient with conjunctivitis developed viral RNA in tears and conjunctive secretions with a very low fever. All other conjunctival swabs were negative, while 55/60 sputum samples were tested positive [16]. A cross-sectional study was conducted with 72 laboratory-confirmed cases where nasopharyngeal and conjunctival samples were collected using synthetic fiber swabs in a mean duration of 18.15 days of disease onset. Conjunctivitis was observed in 2 patients, where only one patient showed PCR positivity in conjunctival swabs. The other patient was a nurse working in the emergency department of ophthalmology, experienced excessive tearing and redness in both eyes with mild to moderate fever, gowned with PPE, including N95 respirators. Still, she gives a history of a dislocated eye mask and frequent hand-eye contact. Her nasopharyngeal and conjunctival swabs were both negative even after 5 days of onset of symptoms. Her diagnosis was confirmed by computerized tomography of the lungs. Her Conjunctivitis was resolved after 4 days and showed no recurrence [17]. In another prospective study

of 17 confirmed COVID-19 patients, tear samples were collected using Schirmers strips weekly starting from day 3 of symptoms to day 30. These were analyzed using RT-PCR assay. It gave negative results in all the cases at all weeks. Among them one of the patients developed conjunctival congestion and chemosis during the hospital stay but showed negative findings in tears [18]. Similar findings were found in a large prospective sample of 114 patients, 80% were positive in their nasopharyngeal swabs. In comparison, none were positive in their conjunctival swab [19], in their conjunctival swabs were negative again in a retrospective analysis of 30 recorded instances of COVID-19 [20].

Mechanism

Ocular Manifestations of Coronavirus in Experimental Animal Models

It has been reported in experimental animal models, the feline coronavirus (feline infectious peritonitis) and the murine coronavirus (mouse hepatitis virus) nare infective. Apart from viral conjunctivitis, they are capable to produce granulomatous anterior uveitis, retinal vasculitis, choroiditis, retinal detachment, virus-induced macular degeneration and optic neuritis with poor prognosis [1]. In a recent study, rhesus macaques were theoretically contaminated with infectious doses of SARS-CoV-2 via the conjunctival sac. Viral load was detectable in the throat, nasal and conjunctival swabs post day 1 of inoculation. Lacrimal glands, the nasolacrimal region, the optic nerve, the alimentary tract, the lower lobe of the lungs were few of the anatomical areas affected. Radiologic investigations showed interstitial pneumonia. Thus, the findings are suggestive of the infection of SARS-CoV-2 via the conjunctival route [21]. Absorption from the ocular tissues like conjunctiva and corneal epithelial, lining of the lacrimal system epithelial cells, and the inner lining is possible. The virus can retrograde into the nasal and ocular fluids. The distribution of cellular receptors in the ocular surface mucosa and the respiratory tract give a chance for higher risk of viral tissue adherence and transmission. The receptors of some species of adenovirus and avian influenza (α-2-3-linked sialic acid, CD 46, desmoglein-2) and the human influenza virus (α-2-6-linked sialic acid) are abundantly present in the corneal, conjunctival epithelium as well as nasal and tracheal mucosal lining [22-24]. The cellular binding receptor, angiotensin-converting enzyme 2 (ACE2) for SARS-CoV and HCoV-NL63 is extensively expressed in the lung alveoli and intestinal epithelial cells. In the eye, ACE2 expressions are found on the corneal, conjunctival epithelium, aqueous and vitreous humor, although less than lungs and gastrointestinal tissues [25,26]. The virus can be transmitted through the lacrimal passage system into the lower respiratory tissues to bind to the ACE2 receptors. The ocular immune system consists of mucous membranes; tears a significant role in the ocular defense mechanisms, therefore the eye can manifest as conjunctivitis and show viral conjunctivitis features as an initial symptom. It has reported that lactoferrinlipocalin 2 and immunoglobin present in the external secretions of saliva, mucous, gastrointestinal fluids, including tears, can inhibit viral attachment by interfering with ACE2 receptors. There is a 150 fold increment in the levels of lactoferrin in SARS –CoV-1patients [25,26]. PCR of the nasopharyngeal swabs is presently the standard for confirmation of COVID-19 [19]. However, the few reported ocular manifestations and test positivity in PCR serve as preliminary evidence of the ocular surface's virus presence. The sensitivity of the PCR test kits is likely to have an impact on the results. False-negative test reports can arise where the viral load is below the detectable range. The inadequate quantity of the sample for that kit [27]. Viral concentrations can also vary at different sample collection sites throughout the disease. According to a report published, the viral load of SARS-CoV detected in the nasopharyngeal swab peaked on the 10th day after the onset of symptoms. Moreover, the study also reported that similar concentrations of viral load were seen in an asymptomatic carrier [28]. Repeated sample collections are usually required to confirm the diagnosis. In any circumstance of repeated negative results in a suspected case, the lungs serve as an alternative diagnostic tool for early diagnosing [29]. Furthermore, the low expressions of ACE2 in the ocular surface are probably another explanation of low or undetectable viral load in the PCR. A Negative report in PCR might not be conclusive for the disease. In the above studies, conjunctivitis and conjunctival swabs' were primarily in the disorder's early phase. Conjunctivitis is usually self-healing within few days and does not seems to have a recurrence. The measurable concentration of the virus in the ocular surface might be for a short period, probably in the early phase, and goes down to undetectable concentrations afterward.

Conclusion

Finding suggests that COVID-19 virus may transmit through the tears by a lacrimal pump mechanism. Information on COVID19 transmission through eye tissues is limited. More scientific trials to establish its occurrence and pathogenic role. Currently, our knowledge about COVID-19 is limited but gradually improving. Anecdotal reports showed preliminary evidence that CoV may or may not transmitted through ocular secretions. The exposed ocular surface can serve as a gateway in transmission and acquiring respiratory diseases. Conjunctivitis is the only reported ocular complication so far, although the incidence is low. Because of the recorded cases of nosocomial transmission and the anatomical and physiological aspects of healthcare workers, it suggested using protective eyewear when examining a confirmed or suspected case of COVID-19to reduces the risk

of occupational exposure. High volume studies are required for specific conclusions. The general population also needs to be conscious regarding the prevention and control of COVID-19.

References

1. Seah I, Agrawal R (2020) Can the Coronavirus Disease 2019 (COVID-19) Affect the Eyes? A Review of Coronaviruses and Ocular Implications in Humans and Animals. Ocul Immunol Inflamm 28(3): 391-395.

2. Sun C, Wang Y, Liu G, Liu Z (2020) Role of the Eye in Transmitting Human Coronavirus: What We Know and What We Do Not Know. Front Public Health 8(1): 155.

3. Dubey G, Khan T, Pant K, Ranjan R, Chaturvedi V, et al. (2020) Eye versus COVID-19 Pandemic: The Hidden Link. IJMSCR 3(3): 725-730.

4. Neha Dubey, Yadav R (2020) Role of Screening and Physiotherapeutic Interventions among COVID-19 Patients in Acute Care Hospital Settings: An Overview. Ijsrm Human 16(2): 23-40.

5. Zhu N, Zhang D, Wang W, Li X, Yang B, et al. (2020) A novel coronavirus from patients with pneumonia in China, 2019. N Engl J Med 382(8): 727-733.

6. Sun K, Chen J, Viboud C (2020) Early epidemiological analysis of the coronavirus disease 2019 outbreak based on crowd sourced data: a population-level observational study. Lancet Digital Health 2(4): 201-208.

7. Li Q, Guan X, Wu P, Wang X, Zhou L, et al. (2020) Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus-Infected Pneumonia. N Engl J Med 382(13): 1199-1207.

8. Van Der Hoek L, Pyrc K, Jebbink MF, Vermeulen Oost W, Berkhout RJM, et al. (2004) Identification of a new human coronavirus. Nat Med 10(4): 368-373.

9. Vabret A, Mourez T, Dina J, Van Der Hoek L, Gouarin S, et al. (2005) Human coronavirus NL63, France. Emerg Infect Dis 11(8): 1225-1229.

10. Loon SC, Teoh SCB, Oon LLE, Se Thoe SY, Ling AE, et al. (2004) The severe acute respiratory syndrome coronavirus in tears. Br J Ophthalmol 88(7): 861-863.

11. Chan WM, Yuen KSC, Fan DSP, Lam DSC, Chan PKS, et al. (2004) Tears and conjunctival scrapings for coronavirus in patients with SARS. Br J Ophthalmol 88(7): 968-969.

12. Hoe NL, Kwai PC, Khan AS, Oon L, Su YST, et al. (2004) Virus-specific RNA and antibody from convalescent-phase SARS patients discharged from hospital. Emerg Infect Dis 10(10): 1745-1750.

13. Yan A (2020) Chinese expert who came down with Wuhan coronavirus after saying it was controllable thinks he was infected through his eyes. South China Morning Post, pp: 12.

14. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, et al. (2020) Clinical Characteristics of Coronavirus Disease 2019 in China. N Engl J Med 382(18): 1708-1720.

15. Zhou Y, Zeng Y, Tong Y, Chen C (2020) Ophthalmologic evidence against the interpersonal transmission of 2019 novel coronavirus through the conjunctiva. medRxiv.

16. Xia J, Tong J, Liu M, Shen Y, Guo D (2020) Evaluation of coronavirus in tears and conjunctival secretions of patients with SARS-CoV-2 infection. J Med Virol 92(6): 589-594.

17. Sun X, Zhang X, Chen X, Chen L, Deng C, et al. (2020) The infection evidence of SARS-COV-2 in ocular surface: A single-center cross-sectional study. medRxiv.

18. Yu Jun IS, Anderson DE, Zheng Kang AE, Wang LF, Rao P, et al. (2020) Assessing Viral Shedding and Infectivity of Tears in Coronavirus Disease 2019 (COVID-19) Patients. Ophthalmology 127(7): 977-979.

19. Deng C, Yang Y, Chen H, Chen W, Chen Z, et al. (2020) Ocular detection of SARS-CoV-2 in 114 cases of COVID-19 pneumonia in Wuhan, China: an observational study. SSRN eLibrary.

20. Xu L, Zhang X, Song W, Sun B, Mu J, Dong X, et al. (2020) Conjunctival polymerase chain reaction-tests of 2019 novel coronavirus in patients in Shenyang, China. medRxiv.

21. Deng W, Bao L, Gao H, Xiang Z, Qu Y, et al. (2020) Rhesus macaques can be effectively infected with SARS-CoV-2 via ocular conjunctival route. bioRxiv.

22. Belser JA, Rota PA, Tumpey M (2013) Ocular Tropism of Respiratory Viruses. Microbiol Mol Biol Rev 77(1): 144-156.

23. Hamming I, Timens W, Bulthuis MLC, Lely AT, Navis GJ, et al. (2004) Tissue distribution of ACE2 protein, the functional receptor for SARS coronavirus. A first step in understanding SARS pathogenesis. J Pathol 203(2): 631-637.

24. Holappa M (2015) Ocular renin-angiotensin system with special reference in the anterior part of the eye. World J Ophthalmol 5(3): 110-124.

25. Lang J, Yang N, Deng J, Liu K, Yang P, et al. (2011) Inhibition of SARS pseudovirus cell entry by lactoferrin binding to heparan sulfate proteoglycans. PLoS One 6(8): 23710.

26. Orr Burks N, Gulley SL, Gallardo RA, Toro H, van Ginkel FW (2014) Immunoglobulin A as an Early Humoral Responder After Mucosal Avian Coronavirus Vaccination. Avian Dis 58(2): 279-286.

27. Chan JFW, Yip CCY, To KKW, Tang THC, Wong SCY, et al. (2020) Improved molecular diagnosis of COVID-19 by the novel, highly sensitive and specific COVID-19-RdRp/Hel real-time reverse transcription-polymerase chain reaction assay validated in vitro and with clinical specimens. J Clin Microbiol 58(5): 310-320.

28. Bhat TA, Kalathil SG, Bogner PN, Blount BC, Goniewicz ML, et al. (2020) An Animal Model of Inhaled Vitamin E Acetate and EVALI-like Lung Injury. N Engl J Med 382(12): 1175-1177.

29. Xie X, Zhong Z, Zhao W, Zheng C, Wang F, et al. (2020) Chest CT for Typical 2019-nCoV Pneumonia: Relationship to Negative RT-PCR Testing. Radiology 292(6): 41-45.