

## Commentary: SARS-CoV-2 in tears: It really matters

Airborne respiratory droplet transmission is well recognized in coronavirus infection; however, ocular secretions, although being held responsible for the spread in many studies, have yet to be proven conclusively.<sup>[1,2]</sup> Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spike proteins bind with the host cellular receptor, human angiotensin-converting enzyme 2, and gain entry into the cell in the presence of transmembrane serine protease 2, a cell surface-associated protease.<sup>[2]</sup> Angiotensin-converting enzyme 2 is known to be expressed on epithelial cells in the lungs, intestines, and kidneys. Recent reports indicate that both angiotensin-converting enzyme 2

and transmembrane serine protease 2 are present in human conjunctival and corneal cells, making the ocular surface cells a potential entry point and reservoir for transmission of the virus.<sup>[3]</sup> The shedding of viral RNA in tears has been observed in both the presence and the absence of ocular manifestations.<sup>[3]</sup>

In this present study, authors have noted the RT-PCR positivity rate of 3.33% from conjunctival samples among 150 patients in their study.<sup>[1]</sup> Arora *et al.*<sup>[4]</sup> included 75 moderate to severe COVID-19-positive patients in their study and found a COVID-19 positivity rate of 24% from tear samples. Kaya *et al.*<sup>[5]</sup> also found a positivity rate of 16% from conjunctival samples. However, Seah *et al.*<sup>[2]</sup> could not detect viral RNA in any of the tear samples of 17 patients. One cross-sectional study by Zhang *et al.*<sup>[6]</sup> showed a 1% positivity rate. In the latter two

studies, they collected the sample in the second and third week. But in the present study, the authors have followed the same procedure as Arora *et al.*<sup>[4]</sup> and collected the sample within 48 hours of collection of nasopharyngeal swab.

In the study done by Arora *et al.*,<sup>[4]</sup> tear samples were collected using conjunctival swabs and Schirmer paper strips. To obtain the conjunctival swab, the lower eyelid was retracted, the inferior fornix of the eye was swept with a sterile nylon swab for 10 seconds, and a similar procedure was repeated in the other eye. Güemes-Villahoz *et al.*,<sup>[7]</sup> Azzolini *et al.*,<sup>[8]</sup> and Kaya *et al.*<sup>[5]</sup> have also collected the sample by conjunctival swab. In this present study, the authors have collected the conjunctival swab sample as described above.

The absence of ocular signs and symptoms in most of the patients with positive conjunctival swabs found in various studies implies that viral shedding in tears is not always related to ocular inflammation, as proposed previously.<sup>[7]</sup> The natural history of conjunctivitis in patients with COVID-19 seems to be self-limiting conjunctivitis that improves in a few days without specific treatment. There was no evidence of corneal infiltrates, membranes, or pseudomembranes. These characteristics differ from the conjunctivitis of other etiologies.<sup>[7]</sup> Study by Güemes-Villahoz *et al.*<sup>[7]</sup> showed that only 17% of the patients with conjunctivitis had severe disease and 33% had mild disease. The present study also showed no significant association between severity of the disease and conjunctival swab positivity, and no association was found between comorbidity and conjunctival swab positivity.<sup>[1]</sup>

Seah *et al.*<sup>[2]</sup> evaluated the possibility of transmission through tears by assessing the presence of SARS-CoV-2 by viral isolation and RT-PCR analysis. A total of 64 samples were obtained during a 3-week period since the onset of symptoms. All samples showed negative results for SARS-CoV-2 on viral isolation and RT-PCR, suggesting that the risk of SARS-CoV-2 transmission through tears is low. Contrary to this, a case report from Italy collected ocular swabs almost daily from a 65-year-old woman with conjunctivitis, detecting SARS-CoV-2 RNA for 18 consecutive days (from days 3 to 21 of the disease), and then 5 days after it became undetectable, the virus was detected again in the ocular swab sample collected at day 27. These findings suggested sustained virus replication in the conjunctiva.<sup>[8]</sup> One important point is that the RT-PCR test does not possess 100% sensitivity; thus, a negative test may represent a false negative result and do not rule out the presence of SARS-CoV-2.

To conclude, conjunctival swab is still a satisfactory method of tear collection for assessment of the presence of SARS-CoV-2 by RT-PCR analysis. Not only the respiratory tract but the precorneal tear film is also one of the transmission routes in patients with moderate to severe COVID-19. Thus, it implies that besides N95 masks, use of gloves, goggles, and face shields by healthcare workers should be mandatory when examining patients with COVID-19 to reduce the transmission of SARS-CoV-2.

## Jyotirmay Biswas, Arkaprava Pradhan<sup>1</sup>

Director, Department of Uveitis and Ophthalmic Pathology,  
<sup>1</sup>Vitreoretina Fellow, Medical Research Foundation,  
Sankara Nethralaya, Chennai, Tamil Nadu, India

**Correspondence to:** Dr. Jyotirmay Biswas,  
Department of Uveitis and Ocular Pathology, Medical  
Research Foundation, Sankara Nethralaya, 18, College Road,  
Nungambakkam, Chennai, Tamil Nadu - 600 006, India.  
E-mail: drjb@snmail.org

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