


Impact of COVID-19 on corneal esthesiometry

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ABSTRACT

Individuals with suspected COVID-19 symptoms (n=202) were tested using nasopharyngeal RT-qPCR. All individuals underwent corneal esthesiometry measurements using the Cochet-Bonnet esthesiometer during their first visit; 50 participants underwent an additional measurement at a mean interval of 32.5 (17.8) days. COVID-19 was confirmed in 101 subjects (50%) using nasopharyngeal PCR. The mean time from symptom onset to disease diagnosis and corneal esthesiometry was 4.2 (2.1) days. Mean corneal esthesiometry findings based on the positive and negative PCR status indicated no statistical difference. This study demonstrated that COVID-19 had no effect on corneal esthesiometry in individuals with acute-phase COVID-19.

BACKGROUND AND METHOD

Besides pneumonia and severe acute respiratory syndrome, which affect patients with COVID-19, other symptoms such as anosmia (22%–68%), dysgeusia (33%) and ageusia (20%) have been frequently reported. These symptoms typically occur in the early stages of the disease and are associated with virus-induced damage to the olfactory and oral mucosal epithelium and olfactory nerve during SARS-CoV-2 invasion and multiplication.¹ According to recent animal studies, demyelination and T cell-mediated autoimmune reactions may occur in the peripheral trigeminal or olfactory nerves causing dysosmia and dysgeusia as a consequence of these nerve injuries.² Previous studies have reported ocular manifestations and detected SARS-CoV-2 RNA in the tear film or conjunctival swabs using RT-qPCR in patients with COVID-19.³ We hypothesised the potential involvement of SARS-CoV-2 in the ophthalmic nerve and its consequent impact on corneal esthesiometry.

This cross-sectional study involved 202 individuals with suspected COVID-19 symptoms; they were examined in an outpatient clinic at the Federal University of São Paulo, Brazil. All individuals were tested for SARS-CoV-2 by nasopharyngeal RT-qPCR (naso PCR) to confirm or exclude COVID-19 diagnosis.

We interviewed patients to identify their date of illness onset and the presence of general signs and symptoms: fever, cough, breathing difficulty, body pain, headache and changes in the sense of smell (anosmia) and taste (dysgeusia).

Information on symptoms such as red eye, tearing, eye discharge, itching and foreign body sensation was also collected. All individuals

underwent slit-lamp biomicroscopy evaluation; the examiner was asked to look for the presence of follicular conjunctivitis.

Corneal esthesiometry measurements were performed using the Cochet-Bonnet esthesiometer (Luneau Ophthalmologie, Paris, France) during patients' first visit. Corneal esthesiometry was analysed based on the naso PCR status, presence of anosmia and dysgeusia, and ocular signs and symptoms.

RESULTS

The mean (SD) age of 202 participants was 37.3 (10.9) years and 67.3% of them were women. The mean time of symptom onset was 4.2 (2.1) days. Naso PCR was performed in all participants during their first visit; 101 (50.0%) were COVID-19 positive.

Fifty participants with positive naso PCR test results underwent a second follow-up visit. The mean interval between the first and second follow-up visits was 32.5 (17.8) days. The SD value for corneal esthesiometry measurement for the right eye at the baseline was 5.52 (0.88) versus 5.60 (0.67) at the second follow-up visit (p=0.616). For the left eye, the SD value for corneal esthesiometry measurement at the baseline was 5.40 (0.80) versus 5.58 (0.67) at the second follow-up visit (p=0.173).

Table 1 depicts the distribution of anosmia and dysgeusia according to the naso PCR status. A high proportion of individuals with both smell (p=0.006) and taste (p=0.032) changes were noted who were positive for COVID-19. However, no differences were noted in their corneal esthesiometry measurements in both eyes according to these symptoms.

No association between ocular symptoms and naso PCR status was noted in this population. Table 2 shows the ocular changes and corneal esthesiometry as stratified by naso PCR results. Individuals' left eye with positive naso PCR showed significantly lower values of corneal esthesiometry for the presence of red eye (p=0.005), tearing (p=0.014) and itching (p=0.011) when compared with those without these symptoms.

Among 202 individuals, 101 (50%) were diagnosed by naso PCR. The study participants' mean time from symptoms onset was 4.2 (2.1) days, indicating that they were tested in their acute disease phase, which, in turn, maximised SARS-CoV-2 RNA detection in the nasopharynx.

Damage to the olfactory epithelium and oral mucosa may explain the occurrence of ageusia, dysgeusia and anosmia observed in the initial



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Table 1 Distribution of anosmia and dysgeusia according to the PCR status and corneal esthesiometry according to the presence of symptoms

	PCR (n=202)		P value
	Negative (n=101)	Positive (n=101)	
Anosmia			0.006
No	70 (57.8)	51 (42.2)	
Yes	31 (38.3)	50 (61.7)	
Dysgeusia			0.032
No	67 (56.3)	52 (43.7)	
Yes	34 (40.9)	49 (59.1)	
	Presence of symptoms		P value
	No	Yes	
<i>Negative PCR</i>			
Anosmia			
CE right eye	5.42 (0.84)	5.32 (0.87)	0.565
CE left eye	5.62 (0.66)	5.54 (0.67)	0.578
Dysgeusia			
CE right eye	5.46 (0.80)	5.26 (0.93)	0.270
CE left eye	5.61 (0.65)	5.58 (0.70)	0.866
<i>Positive PCR</i>			
Anosmia			
CE right eye	5.31 (0.90)	5.62 (0.80)	0.075
CE left eye	5.41 (0.66)	5.64 (0.63)	0.116
Dysgeusia			
CE right eye	5.38 (0.91)	5.55 (0.82)	0.337
CE left eye	5.44 (0.80)	5.61 (0.63)	0.243

*Data are presented as mean (SD) or frequency (proportion).
CE, corneal esthesiometry.

disease stage. However, SARS-CoV-2 has demonstrated a trans-neuronal penetration through the olfactory bulb and its infection has resulted in the rapid transneuronal spread of the virus to the connected areas of the brain in a mouse model of the disease.⁴

Based on several reports providing evidence of SARS-CoV-2 neurotropism and virus migration from the peripheral nerves through the olfactory bulb, leading to a high prevalence of chemosensory dysfunction (anosmia (22%–68%), dysgeusia (33%) and ageusia (20%)),⁵ we analysed the possible ophthalmic nerve damage interfering with corneal esthesiometry.^{3, 6–8} Anosmia and dysgeusia were recorded in 49.5% and 48.5% patients, respectively, based on the positive naso PCR status. These findings are consistent with those reported by Agyeman *et al*, who found 41.0% and 38.2% prevalence of olfactory and gustatory dysfunctions, respectively.⁹ However, we noted no changes in corneal esthesiometry based on these symptoms.

Our study demonstrated no statistical difference in corneal esthesiometry based on the naso PCR status (right eye, $p=0.566$ and left eye, $p=0.420$) in the acute disease phase. Pirraglia *et al* did not detect any changes in corneal esthesiometry in their analyses of 43 hospitalised patients with COVID-19, although it is important to mention that their assessment was performed after a median period of 21.5 days (range: 1–47 days) from hospitalisation.¹⁰ We performed a second corneal esthesiometry evaluation in 50 patients with COVID-19 with a mean interval between the first and second follow-up visit of 32.5 (17.8) days. No statistical difference was noted in comparing the mean value for corneal esthesiometry at the baseline and the second follow-up visit for the right eye ($p=0.616$) and the left eye ($p=0.173$). No association was noted between ocular signs and symptoms and the naso PCR status in this study population.

Table 2 Corneal esthesiometry values in accordance with the presence of ocular signs and symptoms, as stratified by the nasopharyngeal PCR status

	Negative naso PCR (n=101)		
	Presence of ocular changes		P value
	No	Yes	
Red eye			
Right	5.45 (0.81)	5.25 (0.93)	0.287
Left	5.67 (0.63)	5.42 (0.74)	0.100
Tearing			
Right	5.53 (0.79)	5.16 (0.89)	0.050
Left	5.67 (0.62)	5.48 (0.73)	0.178
Eye discharge			
Right	5.38 (0.86)	5.43 (0.81)	0.833
Left	5.57 (0.69)	5.75 (0.44)	0.340
Itchy eyes			
Right	5.45 (0.88)	5.31 (0.80)	0.421
Left	5.66 (0.63)	5.52 (0.69)	0.286
Foreign body sensation			
Right	5.34 (0.87)	5.64 (0.70)	0.183
Left	5.58 (0.69)	5.70 (0.47)	0.491
Follicular conjunctivitis			
Right	5.41 (0.87)	5.34 (0.81)	0.702
Left	5.53 (0.70)	5.72 (0.56)	0.184

	Positive naso PCR (n=101)		
	Presence of ocular changes		P value
	No	Yes	
Red eye			
Right	5.51 (0.85)	5.26 (0.93)	0.261
Left	5.62 (0.66)	5.10 (0.87)	0.005
Tearing			
Right	5.51 (0.84)	5.36 (0.93)	0.414
Left	5.64 (0.57)	5.27 (0.94)	0.014
Eye discharge			
Right	5.47 (0.87)	5.33 (0.86)	0.634
Left	5.53 (0.71)	5.44 (0.88)	0.731
Itchy eyes			
Right	5.53 (0.81)	5.24 (1.01)	0.134
Left	5.65 (0.55)	5.12 (1.01)	0.011
Foreign body sensation			
Right	5.47 (0.87)	5.42 (0.85)	0.865
Left	5.56 (0.71)	5.28 (0.82)	0.187
Follicular conjunctivitis			
Right	5.52 (0.89)	5.33 (0.80)	0.322
Left	5.59 (0.75)	5.40 (0.68)	0.213

Data are presented as means (SD).
naso PCR, nasopharyngeal PCR.

Nevertheless, the esthesiometry was normally independent of the naso PCR status.

In summary, this study demonstrated that SARS-CoV-2 infection did not interfere with corneal esthesiometry, at least, in the mild and early stages of this disease.

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