Received: 26 March 2020 | Revised: 2 April 2020 | Accepted: 13 April 2020

DOI: 10.1111/odi.13365

ORAL DISEASES Leading in Oral, Maxillofacial, Head & Neck Medicine WILEY

LETTER TO THE EDITOR

SARS-CoV-2: What can saliva tell us?

Dear Editor,

An epidemic pneumonia was first reported in the city of Wuhan, China, in the end of December 2019, had its aetiological agent identified as a new coronavirus (Zhu et al., 2020). The World Health Organisation (WHO) declared on 11 March 2020 that the epidemic of the new coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is a pandemic now called COVID-19. Up to now, the number of confirmed cases amounts to approximately 417,000, with more than 18,000 deaths and affecting 196 countries or territories, thus becoming one of the greatest challenges of the contemporary society (https://www.who.int/emergencies/diseases/novel-coronavirus-2019).

The key issue for tracing strategies to control the pandemic relies on testing the highest number of individuals as possible, including the asymptomatic ones, who account for approximately 79% of the spread of the contagion (Li et al., 2020). The traditional collection of upper respiratory tract specimens, such as nasopharyngeal swabs, throat swabs, nasal swabs and lower respiratory tract specimens such as sputum and bronchoalveolar lavage (BAL), has a series of drawbacks regarding collection time, healthcare staff exposure, patient's discomfort, use of specific instruments and mainly, difficulty or impossibility of self-collection, thus being one of the factors limiting the expansion of the tests (Kwon et al., 2020).

Saliva has been shown to be an interesting alternative for detection of viruses as oral shedding is more frequent than viremia (Braz-Silva et al., 2017), so being a fluid with potential diagnostic use (Martelli et al., 2018; Castro et al., 2018), including for respiratory viruses (To et al., 2017; To et al., 2019). The use of saliva, following proper saliva collection and handling high-quality procedures, has a number of advantages, such as less invasiveness, easy collection, possibility of self-collection, less exposure of healthcare workers, shorter execution time, no need of specific instruments, possibility of serial sampling and development of point-of-care devices (Malamud & Rodriguez-Chavez, 2011; Braz-Silva et al., 2017). The concordance rate of nasopharyngeal aspirate and saliva was 93% for influenza and respiratory syncytial virus (To et al., 2019).

Saliva can be relevant also for the fact that in these samples can be investigated the virus in active replicative status, that likely is the transmissible form. Additionally, to date, from the beginning of the pandemic of COVID-19, the rate of viral infected symptomatic peoples globally had an exponential increment during the recent weeks. However, the role of viral molecular feature and the potential genetic changes involved in this high transmission are not well investigated yet. Thus, enrolled saliva samples from different patient at different times can be relevant to investigate molecular genetic changes of transmissible viral form that can be of interest for vaccine and therapeutic antiviral development.

A recent study by one of our research groups investigating the detection of SARS-CoV-2 in serial saliva samples showed positivity in 20 of 23 of the individuals diagnosed based on nasopharyngeal swab and sputum, by reverse transcriptase quantitative PCR assay (RT-qPCR), showing that saliva has an excellent diagnostic potential for COVID-19, in addition to enabling molecular follow-up of these patients (To et al., 2020). Although larger studies are necessary to determine the predictive power of salivary samples, in the present study this method yielded sensitivity of 87% (95% confidence interval, 65%–97%).

The use of saliva for diagnostic purposes opens the possibility of using other tools other than the direct detection of the pathogen, such as the use of proteomic, metabolomics, detection of antibodies, especially IgA, cytokines, chemokines, techniques in order to search for markers enabling the use of rapid diagnostic devices (Malamud & Rodriguez-Chavez, 2011).

In addition to the diagnosis itself, the study of saliva in cases of COVID-19 will help understanding its pathogenesis, since it has been recently reported that epithelial cells of the oral cavity showed abundant expression of the angiotensin-converting enzyme II (ACE2), a receptor playing a key role in the entry of SARS-CoV-2 into the cells (Xu et al., 2020).

The dynamics of nasopharyngeal (Zou et al., 2020) and salivary (To et al., 2020) excretions in hospitalised patients has been described. Therefore, it is extremely important to describe this dynamic in asymptomatic and mildly symptomatic patients sent to home quarantine so that the appropriate period of isolation can be determined. This can only be possible by analysing serial saliva samples, which can be easily self-collected. Moreover, such an approach will provide important information on the transmission routes for establishing protective measures not only for the dental community (Meng et al., 2020), but also for controlling the current pandemic. The support for research involving the study of saliva in countries with foci of COVID-19 is of paramount importance, which can contribute to the application of diagnostic tests to large populations as well as to the understanding of the biological behaviour of the virus.

CONFLICT OF INTEREST

The authors declare that they have no competing interests.

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Paulo Henrique Braz-Silva: Conceptualization; Investigation; Writing-original draft; Writing-review & editing. **Debora Pallos:** Conceptualization; Investigation; Writing-original draft; Writing-review & editing. **Simone Giannecchini:** Conceptualization; Investigation; Writing-original draft; Writing-review & editing. **Kelvin Kai-Wang To:** Conceptualization; Investigation; Writing-original draft; Writing-review & editing.

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