Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Oral Oncology 108 (2020) 104926

Contents lists available at ScienceDirect

Oral Oncology

journal homepage: www.elsevier.com/locate/oraloncology

Letter to the editor

Critical appraisal on salivary diagnostic for COVID-19

We read with great interest an article by Baghizadeh et al. [1] titled "Oral saliva and COVID-19". Authors have comprehensively reviewed all the possible aspects associated with saliva, salivary gland and Novel Corona Virus Disease (COVID-19). Attention has also focused on the use of saliva as a sampling material for diagnosis of acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) infection. However, we would like to express reservations in this regard.

The dire need for saliva based diagnostics for COVID-19 has come in the middle of peak surge of COVID-19 [1,2]. The rationale is highly speculative, which claims that the virus particles possibly come from the respiratory system and infected salivary glands. Proposed advantages are less-invasive, convenience, self-collection and minimum risk of cross infection [1-3]. Bellow are some reality check on it, which are in disagreement with the proposed contention for saliva based diagnostics for COVID-19.

- By using Quality Assessment and Diagnostic Accuracy Tool-2 (QUADAS-2) [4], we have conducted risk of bias assessment and applicability concern for the 5 studies mentioned by the author. (Table 1) Study by Azzi et al. [5] was not included as only two case reports were presented and hence scientifically can not be categorized as original research. Due to improper sampling, case-control design and appropriate blinding of the study group all the five studies were categorized as high risk in both the domains of QUADAS-2 [2,6-9]. Index test and reference standard have used standardized RT-PCR for the detection of SARS-CoV-2 virus particles and hence, were regarded as low risk. Due to unavailability of time interval and any interventions between index test and reference standard all studies were categorized as unclear bias in both the domains of QUADAS-2 [2,6-9]. Based on these findings and fact that sample size was not remarkable in any of the studies, it is not justified to draw any confirmatory and meaningful conclusion about the saliva based COVID-19 diagnostics.
- It is quite conceivable that samples from representative areas have fewer chances of false-negative or false-positive results. By the virtue of abundant angiotensin converting enzyme 2 (ACE2) receptors, respiratory tract is the most commonly affected site and regarded as the representative area for COVID-19. Contrary, authentication of ACE2 expression in oral mucosal cells or salivary glands cells has not been authentically proved with the use of appropriate experimentation at molecular level. Till then viruses in saliva are just a contamination from the respiratory source and hence not a strong justification for development of salivary diagnostic.
- Currently, naso/oropharynx swabs are taken for diagnosis of COVID-19 and till now there are no reported difficulties or shortcoming of the technique reported in the literature. Hence, when naso/oropharynx swabs can be taken with ease then why there is need for salivary sample? Even in a case of trismus or gaging, a swab sample can be obtained from nasal cavity.
- Low risk of contamination has been speculated for salivary samples. Personal protection kit is mandatory for obtaining any kind of samples from suspected cases of COVID-19. In that case, the risk of cross infection to health personnel remains equal for salivary and naso/oropharynx samples.
- Finally, is 'self-collection of salivary sample' a remarkably significant criterion for future in-depth investigation?

Table 1
Risk of bias and applicability concern analysis of included studies using Quality Assessment and Diagnostic Accuracy Tool-2.

Domains	Patient Selection	Index Test	Reference Standard	Flow and Timing
Risk of bias arm				
Azzi et al. [6]	High	Low	Low	Unclear
To et al. [7]	High	Low	Low	Unclear
Chen et al. [8]	High	Low	Low	Unclear
To et al. [2]	High	Low	Low	Unclear
Williams et al. [9]	High	Unclear	Low	Unclear
Applicability concern arm				
Azzi et al. [6]	High	Low	Low	–
To et al. [7]	High	Low	Low	–
Chen et al. [8]	High	Low	Low	–
To et al. [2]	High	Low	High	–
Williams et al. [9]	High	Unclear	Low	–

In conclusion, salivary diagnostic for COVID-19 infection does not show substantial evidence for effective implementation in the current situation. Highly speculative nature of the proposed merits questions its utility in future. Since, currently available diagnostic modalities and self sufficient, future efforts and time should be devoted more towards exploring pathogenesis and therapeutics for COVID-19 infection.

Funding source
None declared.

Declaration of Competing Interest

The authors declared that there is no conflict of interest.

https://doi.org/10.1016/j.oraloncology.2020.104926
Received 17 July 2020; Accepted 20 July 2020
Available online 22 July 2020

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