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Review Article

Saliva: In Relation to COVID19

Manal Abdalla Eltahir BDS, MD, MFDRCSI, FIBCSOMS*

Assistant Professor, Faculty of Dentistry, Department of Oral and Maxillofacial Surgery and Diagnostic Sciences, Qassim University, KSA

***Corresponding Author:** Manal Abdalla Eltahir, Assistant Professor, Faculty of Dentistry, Department of Oral and Maxillofacial Surgery and Diagnostic Sciences, Qassim University, KSA.

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Abstract

COVID19, as it designated by WHO, infection outbreak is constitute a real disaster worldwide, from December 2019 to April 2020, the number of affected individuals is more than the million victims. This short review aimed to gather information in the form of answering important questions in the context of Saliva in relation to COVID19 Which is caused by SARS-CoV2, as an emergent infection with limited information about. These questions are: is saliva just an environment facilitates the viral transmission?, How the saliva gets infected with corona virus? what is the actual role of the ACE2 receptors express in the oral cavity in the context of the pathogenesis of COVID-19 disease? What is the life span of the virus in saliva? and What is the role of antiviral components of saliva in combating of the coronavirus?

Keywords: Corona Virus; Saliva-ACE2-Antiviral; COVID19

Corona Virus

Coronaviruses are a group of viruses belonging to the *Coronaviridae* family [1] which is RNA enveloped viruses [2] COVID-19, as it designated by WHO [3], is an emergent infection, which is started in Wuhan China December 2019 with continuing its spread throughout the world [4] till the time of writing this review April 2020. The disease is ranging from mild to severely lethal in some cases [1], while which factors contribute to this severity and Fatality, are differ from country to others and from patient to other as some reports showed that it is depending on preparedness and availability of health care [5] and furtherly the fade of disease is seem to be affected widely by the presence of co-morbid diseases [6].

The incubation period of 2019-nCov, nearly similar to the incubation period of Middle East respiratory syndrome coronavirus (MERS-CoV), which it has been estimated to be 5 to 6 days on average [7], but there is evidence that it could be as long as 14 day [8], which is now the commonly adopted duration for quarantine of exposed persons [9].

Many numbers of corona viruses, varied in their sensitivity to pH, but still they are more stable at slightly acidic pH (6 - 6.5) than at alkaline pH [10,11], which matching or near the normal pH of saliva (6 to 7) [12].

Saliva

Saliva is a complex isotonic substance, gains its hypotonicity as it travels through the ductal system [13]. It has only one seventh the tonicity of normal interstitial fluids [14,15]. Water constitutes 99% of saliva, while the other Constituents constitutes 1% [16]. In a heathy individual, average salivary flow per day is range between (1-1.5 L) [17].

For detection of respiratory viruses, including coronaviruses, saliva has a high concordance rate of greater than 90% with nasopharyngeal specimens [18,19], moreover, In some patients, coronavirus was detected only in saliva but not in nasopharyngeal aspirate [18,20].

Source of the virus in saliva

Viral transmission from person to person is well documented [21].

It was suggested (Figure 1), that, the presence of 2019-nCoV in patients' saliva, is either from:

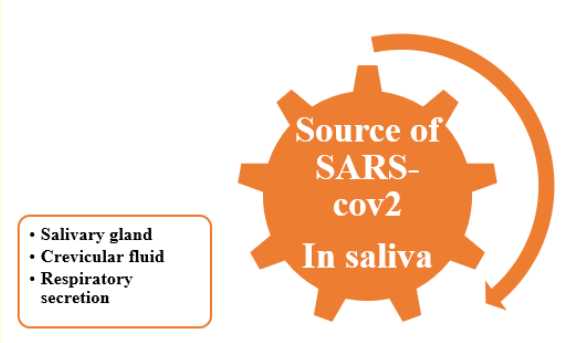

Figure 1: Suggested source of SARS-CoV2 in saliva.

- Salivary gland infection followed by release of the viral's particles in saliva [22]
- Virus coming from More than one source: oral saliva, nasopharyngeal secretion as well as lower respiratory tract secretion, for the reason that, oral Saliva specimens containing secretion of salivary glands and at the same time containing coming down secretion from nasopharynx or coming up by the airway ciliary action from the lung.
- COVID-19 present in the infected blood, can access the mouth via crevicular fluid, an oral cavity-specific exudate.

More studies are needed to determine the source of the virus in saliva [23].

Diagnosis of COVID19, by using saliva specimen (Figure 2)

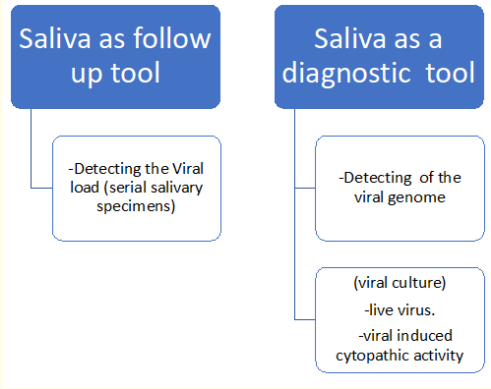

Figure 2: Saliva Specimen for both diagnosis and follow up of SARS-CoV2.

For detection of respiratory viruses, saliva has a high concordance rate of greater than 90% with nasopharyngeal specimens [18,19]. Recent study showed great percentage (91.7%) for self-collecting saliva specimen in detection of SARS-CoV2, moreover in some patients, coronavirus was detected only in saliva rather than nasopharyngeal aspirate [18,20].

SARS-CoV-2 RNA could be detected in saliva, for up to 20 days [24].

Turning from the past concept of theoretical, potential diagnosis to present and future, actual and practical diagnosis; saliva can be used for both diagnostic and follow up (serial saliva specimens for detecting the viral load) purposes [23].

2 types of test can be done for the COVID19 virus detection in saliva:

- Nucleic Acid Extraction and Real-time Reverse Transcription-Quantitative Polymerase Chain Reaction for 2019-nCoV, by detecting of genetic material of the virus.
- Viral culture; can demonstrate the live virus, and Virus-induced cytopathic effect which can be examined daily up to 7 days.

Saliva as specimen for diagnosis of COVID19 is advantageous for the reasons that (Figure 3):

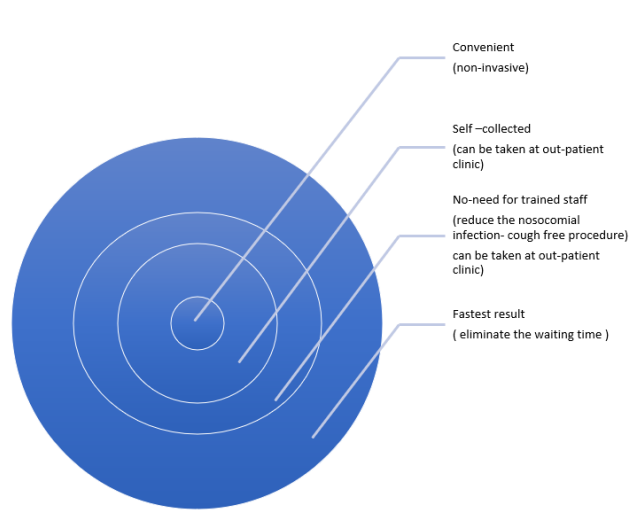

Figure 3: The advantages of saliva as specimen in SARS-CoV2.

- It is a convenient, non-invasive procedure, which can reduce the nosocomial transmission; as the procedure is a cough free not like nasopharyngeal swab [25] as well as reduction of discomfort especially for repeatable specimen using nasopharyngeal or oropharyngeal swab.

- Saliva can be used as a self -collection, specimen, so no need for trained personnel, which can eliminate the waiting time for specimen collection as well as allowing the test to be taken at –outpatient clinics that will enable fastest results [23].

Antiviral components in saliva

Saliva, in human being due to the presence of certain physical, chemical and physicochemical agents has got a noticeable property in protection of the oral tissues against harmful compound which are produced by greater number of microorganisms [26].

Certain immunologic and non- immunologic proteins in saliva have got an antiviral activity [27], such as: Cathelicidin, (LL-37), Lactoferrin, Lysozyme, Mucins, Peroxidase, Salivary agglutinin (gp340, DMBT1), SIgA (secretory IgA), SLPI (secretory leucocyte protease inhibitor), and α, β Defensins [28].

The presence of the infectious viruses such as SARS-cov2,in the oral cavity despite the presence of such antiviral activities, which will lead furtherly for the spread of the infection, may be explained by the couple of reasons that were mentioned previously in literature: that most of the antiviral substances in saliva have relatively limited antiviral potency and a little bit of restricted mode of action, the other reason that the concentration of the antiviral salivary proteins differ from person to person [29]; even those with a heathy individuals that is influenced by age, gender as well as diet [30], salivary proteins (antiviral substance as part of this proteins) can be affected by previous factors in addition to other elements such as, inflammation, infection,, stress as well as hormonal changes [13,31] and that exhibit the interaction of antiviral according to systemic conditions, as well as the oral cavity ecology [32]. In addition to that the presence of a variety of microorganisms with the diversity in bioactivities in the oral cavity may explain this activity [33].

Furtherly, presence of the virus in saliva may be behind the GIT symptoms (diarrhea, vomiting) reported in few affected cases [34] following of swallowing of such infected saliva.

Virus and ACE2 receptors in oral cavity

Angiotensin converting enzyme 2 (ACE2) a membrane-associated aminopeptidase, which has got expression in many organs of human body (vascular endothelia, renal and cardiovascular tissue, and epithelia of the small intestine and testes [35-37]. It plays multiplicity of functions in the organs that expressed on [39] abnormal expression has been implicated in diabetes, hypertension and heart failure [38].

Molecular Structure similarity between the emerging virus SARS -CoV2, and the other virus of 2003's outbreak namely SARS.-CoV1, at the level of receptor-binding domains strongly suggested that the entry of the virus is through ACE2 receptor [39], furtherly, binding of the virus to the ACE2 receptor can induce certain immunoreactions, and the receptor diversity between humans and animal species designated as SARS-CoV-2 reservoirs furtherly increases the complexity of COVID-19 immunopathogenicity [40,41].

Recent results showed that the ACE2 could be expressed in the oral cavity and was highly enriched in epithelial cells. Moreover, among different oral sites, ACE2 expression was higher in tongue

than buccal and gingival tissues. These findings indicate that the Oral mucosa, may be a potentially high-risk route of 2019-nCov infection [42,43]. By so far searching the literature we couldn't find a report have explained, shall the virus induce oral symptoms? so is seem to be that this point is no longer investigated.

Conclusion

More than one point are discussed in this review for saliva in relation to the COVID19 virus, although not all the answers for questions are totally conclusive, just we aimed to reflect the light on these points for the saliva as promising tool in both diagnostic and follow up for COVID 19 virus, as a convenient. and a practical tool. Many researches would be anticipated for putting clear answers for the mentioned questions.

Bibliography

1. www.who.int›who-rights-roles-respon-hw-covid-19
2. Chloé Geller., *et al*. "Human Coronaviruses: Insights into Environmental Resistance and Its Influence on the Development of New Antiseptic Strategies". *Viruses* 4 (2012): 3044-3068.
3. https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200211-sitrep-22-ncov.pdf?sfvrsn=fb6d49b1_2
4. Hussin A Rothan and Siddappa N Byrareddy. "The epidemiology and pathogenesis of coronavirus disease (COVID-19) outbreak". *Journal of Autoimmunity* 109 (2020): 102433
5. Likelihood of survival of coronavirus disease 2019.
6. Guan W-jie., *et al*. "Comorbidity and its impact on 1590 patients with Covid-19 in China: A Nationwide Analysis". *European Respiratory Journal* (2020).
7. Backer Jantien A., *et al*. "Incubation period of 2019 novel coronavirus (2019-nCoV) infections among travellers from Wuhan, China, 20-28 January 2020". *Eurosurveillance* 25.5 (2020): pii=2000062.
8. Xiao-Wei Xu., *et al*. "Clinical findings in a group of patients infected with the 2019 novel coronavirus (SARS-Cov-2) outside of Wuhan, China: retrospective case series". *BMJ* 368 (2020): m606.
9. Backer JA., *et al*. "Incubation period of 2019 novel coronavirus (2019-nCoV) infections among travellers from Wuhan, China, 20-28 January 2020". *Eurosurveillance* 25.5 (2020).
10. Fouchier RA., *et al*. "A previously undescribed coronavirus associated with respiratory disease in humans". *Proceedings of the National Academy of Sciences of the United States of America* 101 (2004): 6212-6216.
11. LAWRENCE S., *et al*. "Conformational Change of the Coronavirus Peplomer Glycoprotein". *Journal of Virology* 64.6 (1990): 3042-3050.
12. Benn A M L and Thomson W M. "Saliva: an overview". *New Zealand Dental Journal* 9 (2014): 92-96.
13. Sue P Humphrey., *et al*. "A review of saliva: Normal composition, flow, and function". *Journal of Prosthetic Dentistry* 85 (2001): 162-169.
14. M Villiger., *et al*. "Evaluation and review of body fluids saliva, sweat and tear compared to biochemical hydration assessment markers within blood and urine". *European Journal of Clinical Nutrition* 72 (2018): 69-76.
15. Ben-Aryeh H., *et al*. "Composition of whole unstimulated saliva of healthy children: changes with age". *Archives of Oral Biology* 35 (1990): 929-931.
16. Edgar WM. "Saliva: its secretion, composition and functions". *British Dental Journal* 172 (1992): 305-312.
17. Gabriela Iorgulescu. "Saliva between normal and pathological. Important factors in determining systemic and oral health". *Journal of Medicine and Life* 2.3 (2009): 303-307.
18. To KK., *et al*. "Additional molecular testing of saliva specimens improves the detection of respiratory viruses". *Emergency Microbes Infection* 6 (2017): e49.
19. To KKW., *et al*. "Saliva as a diagnostic specimen for testing respiratory virus by a point-of-care molecular assay: a diagnostic validity study". *Clinical Microbiology Infection* 25 (2019): 372-378.

20. To KK., *et al*. "Additional molecular testing of saliva specimens improves the detection of respiratory viruses". *Emergency Microbes Infection* 6 (2017): e49.

21. Li P., *et al*. "Transmission of COVID-19 in the terminal stage of incubation period: a familial cluster". *International Journal of Infectious Diseases* (2020).

22. Robinson Sabino-Silva. "Coronavirus COVID-19 impacts to dentistry and potential salivary diagnosis". *Clinical Oral Investigations* (2020).

23. To KKW., *et al*. "Consistent Detection of 2019 Novel Coronavirus in Saliva". *Clinical Infection Disease* (2020).

24. Kelvin Kai-Wang To., *et al*. "Temporal profiles of viral load in posterior oropharyngeal saliva samples and serum antibody responses during infection by SARS-CoV-2: an observational cohort study". *The Lancet* (2020).

25. Joan L Robinson., *et al*. "Use of Throat Swab or Saliva Specimens for Detection of Respiratory Viruses in Children". *Clinical Infectious Diseases* 46 (2008): 61e-64e.

26. Jorma Tonovuo. "Antimicrobial function of human saliva - how important is it for oral health?" *Acta Odontologica Scandinavica* 7 (2009): 250-256.

27. Patricia Del Vigna de Almeida., *et al*. "Saliva Composition and Functions: A Comprehensive Review". *The Journal of Contemporary Dental Practice* 9 (2008).

28. C Dawes AML., *et al*. "The functions of human saliva: A review sponsored by the World Workshop on Oral Medicine". *Archives of Oral Biology* 60 (2015): 863-874.

29. MR White., *et al*. "Multiple components contribute to ability of saliva to inhibit influenza viruses". *Oral Microbiology Immunology* 24 (2009): 18-24.

30. Kashi Raj Bhattaral., *et al*. "Compliance with Saliva Collection Protocol in Healthy Volunteers: Strategies for Managing Risk and Errors". *International Journal of Medical Sciences* 15.8 (2018): 823-831.

31. Rudney JD. "Does variability in salivary protein concentrations influence, oral microbial ecology and oral health?" *Critical Reviews in Oral Biology and Medicine* 6 (1995): 343-367.

32. D Malamud., *et al*. "Antiviral activity of Human Saliva". *Advances in Dental Research* 23.1 (2011): 34-37.

33. Zhang H., *et al*. "The digestive system is a potential route of 2019-nCov infection: a bioinformatics analysis based on single-cell transcriptomes". *bioRxiv* (2020).

34. Hamming I., *et al*. "Tissue distribution of ACE2 protein, the functional receptor for SARS coronavirus. A first step in understanding SARS pathogenesis". *Journal of Pathology* 203 (2004): 631-637.

35. Donoghue M., *et al*. "A novel angiotensin-converting enzyme-related carboxypepti- dase (ACE2) converts angiotensin I to angiotensin 1-9". *Circulation Research* 87 (2000): e1-e9.

36. Harmer D., *et al*. "Quantitative mRNA expression profiling of ACE 2, a novel homologue of angiotensin converting enzyme". *FEBS Letter* 532 (2002): 107-110.

37. Anthony J Turner. "Chapter 25, ACE2 Cell Biology, Regulation, and Physiological Functions". *The Protective Arm of the Renin-Angiotensin System (RAS)* (2015): 185-189.

38. Chih-Fong Chou., *et al*. "ACE2 orthologues in non-mammalian vertebrates, (Danio, Gallus, Fugu, Tetraodon and Xenopus)". *Gene* 377 (2006): 46-55.

39. Y Wan., *et al*. "Receptor recognition by novel coronavirus from Wuhan: an analysis based on decade-long structural studies of SARS". *Journal of Virology* (2020).

40. Čivljak., *et al*. "The third coronavirus epidemic in the third millennium: what's next?" *Croatian Medical Journal* 61 (2020): 1-4.

41. Zihao y. "The diverse of Ace2 receptor made the inference of host difficult. copy.pdf. figshare. Preprint" (2020).

42. Hao Xu., *et al*. "High expression of ACE2 receptor of 2019-nCoV on the epithelial cells of oral mucosa". *International Journal of Oral Science* 12 (2020): 8.

43. Roujian Lu., *et al*. "Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding". *Lancet* 395.10224 (2020): 565-574.