LETTER TO THE EDITOR

Prevalence of dry mouth in COVID-19 patients with and without Sicca syndrome in a large hospital center

Joseph Katz

Received: 23 November 2020 / Accepted: 14 December 2020 / Published online: 12 January 2021

The ACE-2 receptor is abundantly expressed on the epithelial cells of the salivary glands, and when infected by SARS-CoV2, these receptors are over expressed [1]. It is speculated that signaling of the ACE-2 receptor by the virus triggers a cascade of inflammatory processes, ending in acute and chronic sialoadenitis and causing disruption in salivary secretion and dry mouth [2, 3].

However, there is a dearth of information on the extent of the association between COVID-19 and dry mouth. Most of the existing literature is comprised of individual case reports or surveys reporting on symptoms from COVID-19 patients [4, 5]. It was suggested that the reported xerostomia is caused by fibrosis repairment [4] or due to the neuroinvasive and neurotropism potential of SARS-CoV-2 [6].

COVID-19 is an infectious disease with a strong inflammatory response as demonstrated by the phenomenon of “cytokines storm” [7]; therefore, it is intriguing to speculate that the reports on positive SSA antibodies in these patients [8, 9] may indicate the existence of autoimmune inflammatory response similar to the one described in Sjogren’s syndrome [10, 11] that can result in dry mouth as well.

The purpose of the present study was to evaluate the prevalence of the association between COVID-19 and dry mouth in Sicca and non-Sicca patients, as well as to evaluate the association between SSA and COVID-19 and CRP and COVID-19.

The study was exempted by the University of Florida Institutional Review Board (IRB).

We used the University of Florida Health Center Integrated Data i2b2 provided by the University of Florida Health Office of the Chief Data Officer for the period of June 2015–September 2020. Diagnoses of COVID-19 (ICD10 U07.1), Sicca syndrome (ICD10 M35.0), Dry mouth (ICD10, R62.8), positive SSA antibody (CPT 86235), elevated CRP (CPT 86140), and total hospital population by age and sex were searched by using the appropriate international classification of diseases (ICD 10). The total hospital population was 98,784,9 patients, 46% male and 54% females. From 889 patients that were diagnosed with COVID-19, 43% were male and 57% were females. A total of 1,772 (0.18%) of patients were diagnosed with dry mouth, 30% were males and 70% females. Nine patients (1.01%) were diagnosed with both COVID-19 and dry mouth. Most of the patients were adults and 100% of both COVID-19 and dry mouth were adults (Table 1).

The OR for COVID-19 with dry mouth was 5.153 (95% CI 2.9220 to 10.9008, \( p \) < 0.001). The OR for COVID-19 in the presence of Sicca syndrome dry mouth was 2.01, not statistically significant (0.7525 to 5.3753, \( p \) = 0.1636). The OR for COVID-19 in the presence of non-Sicca dry mouth was 3.5661 (95% CI 1.4786 to 8.6009, \( p \) = 0.0046) (Table 2). The OR for COVID-19 in the presence of positive SSA was 2.2519 (95% CI 1.2418 to 4.0835, \( p \) = 0.0075. The OR for COVID-19 in the presence of elevated CRP was 4.3237 (95% CI 2.0523 to 9.1091, \( p \) < 0.0001) (Table 3).

| Table 1 Demographic data of patients with dry mouth in COVID-19, COVID-19 patients only, dry mouth in hospital patients, and all hospital patients |
|---|---|---|---|---|
| | Dry mouth and COVID-19 | COVID-19 | Dry mouth (ICD10 R68.2) | Hospital |
| Total | 6 | 889 | 1772 | 987849 |
| Male | 0 | 385 (43%) | 534 (30%) | 455230 (46%) |
| Female | 6 (100%) | 504 (57%) | 1238 (70%) | 532165 (54%) |
| Children | 0 | 38 | 151 | 156063 |
| Adults < 18 years | 6 (100%) | 851 (96%) | 1621 (91%) | 831786 (84%) |

Joseph Katz
jkatz@dental.ufl.edu

1 Department of Oral & Maxillofacial Diagnostic Sciences, University of Florida College of Dentistry, Gainesville, FL, USA
Dry mouth is a condition that may result from many causes, including autoimmune, endocrine and neurological conditions, and the use of a variety of medications. In addition, it is clear that the intensive medical therapies especially in intensive care units may contribute significantly to the subjective and objective complaints of dry mouth.

Several studies of self-reported complaints of COVID-19 patients have documented oral symptoms such as dry mouth and dysgeusia [4, 5]. Few authors have suggested that SARS-CoV-2 binds to ACE-2 receptors on the epithelium of salivary glands, replicate, lyse cells, and propagate signs and symptoms, such as discomfort, inflammation, and pain in major salivary glands and resulting in chronic sialoadenitis [2, 3]. Some authors have suggested that the dry mouth results from the neurotoxic effects of the virus on target organs with effects on CNS [4].

Patients with rheumatic diseases are known to be at higher risk of infections such as COVID-19. This might be attributed to their rheumatic disease activity, comorbidities, and immunosuppressive therapy [12]. COVID-19 shares a similar inflammatory immune response with autoinflammatory and autoimmune conditions. Viruses can share immune responses with autoimmune diseases such Kawasaki disease, vasculitis, and Sjögren’s-like syndrome [9, 13].

In conclusion, dry mouth related to Sicca and not related to Sicca are strongly associated with COVID-19. The causes for this association are not clear and may include autoimmunity causes as well as increased risk for infection and the impact of other comorbidities and therapies. Clinician should be aware of the association and treat the patients accordingly.

### Compliance with ethical standards

The study was exempted from approval by the Institutional Review Board (IRB) of the Health Center at the University of Florida as it does not involve any disclosure of personal health information (PHI). All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

This article does not contain any studies with animals performed by any of the authors.

### Ethical approval

This article does not contain any studies with human participants or animals performed by any of the authors.

### Conflict of interest

Dr. Katz is a consultant for HT Bioimaging on an unrelated project.

### References

1. Liu L, Wei Q, Alvarez X, Wang H, Du Y, Zhu H, Jiang H, Zhou J, Lami P, Zhang L, Lackner A, Qin C, Chen Z (2011) Epithelial cells lining salivary gland ducts are early target cells of severe acute respiratory syndrome coronavirus infection in the upper respiratory tracts of rhesus macaques. J Virol 85(8):4025–4030. https://doi.org/10.1128/JVI.02292-10
2. Baghizadeh Fini M (2020) Oral saliva and COVID-19. Oral Oncol 108:104821. https://doi.org/10.1016/j.oraloncology.2020.104821
3. Wang C, Wu H, Ding X, Ji H, Jiao P, Song H, Li S, Du H (2020) Does infection of 2019 novel coronavirus cause acute and/or chronic sialadenitis? Med Hypotheses 140:109789. https://doi.org/10.1016/j.mehy.109789
4. Fantozzi PJ, Pampena E, Di Vanna D, Pellegrino E, Corbi D, Mammucari S, Alessi F, Pampena R, Bertazzoni G, Minisola S, Mastroianni CM, Polimeni A, Romeo U, Villa A (2020) Xerostomia, gustatory and olfactory dysfunctions in patients with COVID-19. Am J Otolaryngol 41(6):102721. https://doi.org/10.1016/j.amjoto.2020.102721
