



## Post-acute infection syndrome after COVID-19: effects on the oral and maxillofacial region and the recent publication trends

Joo-Young Park, DDS, PhD<sup>1,2</sup>

Associate Editor of JKAOMS

<sup>1</sup>Department of Oral and Maxillofacial Surgery, Seoul National University Dental Hospital, School of Dentistry, Seoul National University;

<sup>2</sup>Oral Mucosa and Jawbone Experimental Immunology Laboratory, Seoul, Korea

The global COVID-19 (coronavirus disease 2019) pandemic that began in late 2019 has caused more than 535 million infections and 6 million deaths as of June 2022<sup>1</sup>. Although the number of newly confirmed cases has been fallen below as 10,000 per day in South Korea, those who have been infected and survived experience long-lasting medical consequences. Those post-infection symptoms were defined as post-acute infection syndrome (PAIS) or post-acute sequelae of COVID-19 (PASC) in the literature<sup>2,3</sup>, and the number of scientific publications dealing with PAIS and PASC has been dramatically increasing since 2020.

Frequently reported residual effects from SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) include fatigue, dyspnea, chest pain, persistent loss of taste and/or smell, cognitive changes, arthralgias, and decreased quality of life<sup>4,5</sup>. With a variety of clinical presentations and degrees of severity in patients, it is necessary for oral and maxillofacial surgeons to understand the emergent effects of PAIS and PASC. In fact, PAIS after viral infections such as Dengue, Ebola, and EBV (Epstein-Barr virus) has been identified long time ago, and all kinds of non-viral infections, including bacteria and parasites, have been implicated in PAIS pathogenesis<sup>6</sup>. Unfortunately, the association between acute infectious diseases and unexplained disability remains understudied, which leads to poor recognition of these conditions in clinical

practice<sup>2</sup>. Besides, as the pandemic emerged in 2019, most studies have been limited in the duration of observation<sup>7</sup>. As a result, patients might experience delayed or a complete lack of clinical care in case of PAIS. Therefore, particular attention on the pathogenesis or the treatment needs for PAIS and PASC has been made very recently by medical scientists and clinicians<sup>2,3</sup>.

Importantly, PAIS after COVID-19 is not only associated with the systemic, respiratory, and neurological symptoms, but also related to pathology in the oral and maxillofacial region. During the second wave of the COVID-19 pandemic, a sudden and rapid rise in rhino-orbital-cerebral mucormycosis incidence was observed and has been identified as a deadly complication of this viral infection<sup>8</sup>. Because of the sudden, rocket high incidence in a brief period, it was defined as COVID-19 associated mucormycosis (CAM) especially affecting maxilla and adjacent facial tissues<sup>8-10</sup>. Before the outbreak of the COVID-19 pandemic, global prevalence of mucormycosis was as low as 0.005 to 1.7 per million population<sup>11</sup>; however, the prevalence is 80 times higher than that recorded in developed countries after COVID-19<sup>12</sup>. Pathogenesis of CAM is currently understood as an opportunistic fungal infection where the immune cells in the SARS-CoV-2 infected host defense differently against commensal or invaded fungal colony<sup>13</sup>. Interestingly, other kinds of opportunistic infections have been reported in the oral and maxillofacial region as PAIS, such as worsened periodontitis, avascular necrosis of jaw, and various spectrum of oral mucositis<sup>8-19</sup>. (Table 1) One of the suggested mechanisms of those oral and maxillofacial manifestations is the direct vulnerability of the oral mucosa to SARS-CoV-2 infection. These are reported to be a consequence of the high ACE-2 expression in the epithelial cells of the oral mucosa<sup>15,19</sup>; however, further study with larger number of clinical cases is required to fully support the hypothesis.

### Joo-Young Park

Department of Oral and Maxillofacial Surgery, Seoul National University Dental Hospital, School of Dentistry, Seoul National University, 101 Daehak-ro, Jongno-gu, Seoul 03080, Korea  
TEL: +82-2-2072-4498

E-mail: bbyoung1@snu.ac.kr

ORCID: <https://orcid.org/0000-0002-0333-6349>

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**Table 1.** The manifestations of PAIS (post-acute infection syndrome) after COVID-19 presented in the oral and maxillofacial region

Diagnosis	The recent publications (reference No.)
Rhino-orbital-cerebral mucormycosis, COVID-19 associated mucormycosis (CAM)	8-13
Worsened periodontitis, ulcero-necrotic gingivitis	15,16
Avascular osteomyelitis of maxilla	14,18
Ulcerative oral mucosal lesions, petechiae, macules, blisters, oral thrush with unknown etiology after COVID-19	15,19

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Nonetheless, the overlap of symptoms, signs, and general features of the individual PAIS and the related oral and maxillofacial pathologies suggest the involvement of shared pathological pathways and the possibility that common diagnostic markers might be established. In addition to basic biomedical and dental research, more needs to be done to refine diagnostic criteria and obtain more reliable estimates of the PAIS prevalence. Moreover, the oral and maxillofacial surgeons need to call for unified nomenclature and better conceptualization of PAIS in the maxillofacial region, leading to the increased scientific publications in this field.

### Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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