

## Can Apical Periodontitis Exacerbate Covid-19 Damage?

Umut Aksoy<sup>1\*</sup>, Ahmet Özer Şehirli<sup>2</sup>, Serkan Sayiner<sup>3</sup>

<sup>1</sup>Near East University, Faculty of Dentistry, Department of Endodontics, Near East Avenue, Lefkosa, 99138, Mersin 10, Turkey.

<sup>2</sup>Near East University, Faculty of Dentistry, Department of Pharmacology, Near East Avenue, Lefkosa, 99138, Mersin 10, Turkey.

<sup>3</sup>Near East University, Faculty of Veterinary Medicine, Department of Biochemistry, Near East Avenue, Lefkosa, 99138, Mersin 10, Turkey.

\*Correspondence to: Umut Aksoy (E-mail: umut.aksoy@neu.edu.tr)

(Submitted: 02 December 2021 – Revised version received: 10 December 2021 – Accepted: 16 December 2021 – Published online: 26 December 2021)

Dear Editor,

The COVID-19 pandemic remains an important health problem, potentially worsened by emerging mutant strains. Although vaccination studies have been rapidly carried out, the definitive treatment protocol for the disease has not yet been established. Therefore, treatment suggestions and studies continue to have importance.

Until the end of the 1980s, the systemic effects of dental infections were ignored except in immunodeficient patients. Later studies revealed a relationship between dental infections and myocardial and cerebral infarction, increasing research interest in this topic.<sup>1-2</sup>

The relationship between periodontitis – which has an important role in dental infections – and systemic diseases has been determined. Although the studies in this area have increased,<sup>3,4</sup> the relationship between apical periodontitis and systemic disease has not yet been completely established.

The periapical infections caused by intracanal microorganisms ensure the secretion of inflammatory cytokines and might accelerate systemic diseases by causing inflammation in distant organs. COVID-19 infection might be accompanied by the excessive production of proinflammatory cytokines, also called “cytokine storm”.<sup>5</sup> The already increased circulatory proinflammatory cytokines in people with apical periodontitis might aggravate the COVID-19 disease by triggering the cytokine storm and might worsen prognosis.

Apical periodontitis is a common infectious disease worldwide; it is also the most frequent inflammatory lesion in the jaw related to the teeth.<sup>6</sup> Apical periodontitis is characterized by an inflammatory response and bone destruction in the periapical tissues resulting from both bacterial infections in the dental pulp and immune response as part of the body's defensive reaction. Epidemiological studies worldwide indicate that apical periodontitis is a widespread oral health problem that could threaten the general health of the population.<sup>7</sup>

Because high serum acute reactive phase proteins were found in those with apical periodontitis, this disease was

thought to be systemic. Indeed, it was shown to be associated with high levels of tumour necrosis factor-alpha (TNF- $\alpha$ ), interleukin 1 (IL-1), interleukin 2 (IL-2), interleukin 6 (IL-6), and interferon-gamma (IFN- $\gamma$ ) in the serum. Aksoy et al.<sup>2</sup> have shown that the activities of two serum matrix metalloproteinases (MMP1 and MMP2) were increased in rats with apical periodontitis compared to healthy rats. Şehirli et al.<sup>8</sup> showed that in those with apical periodontitis, serum levels of lactate dehydrogenase, alkaline phosphatase, and creatine kinase increased while superoxide dismutase activity decreased, resulting in structural damage to heart tissue. Apical periodontitis affects T helper cells, activating macrophages. The increase in cytokine expression is thought to increase sensitivity in people with systemic damage.

After coronavirus disease 2019 (COVID-19) infection, people can undergo severe tissue damage resulting from the increased expression of cytokines such as TNF- $\alpha$ , IL-1, IL-6, and IFN- $\gamma$ . It appears that COVID-19 activates various inflammatory pathways together with oxidative stress, thus producing intense inflammation in tissues such as the lung, heart, brain, stomach, intestine, and kidney.<sup>9</sup> Because of the reported increased expression of cytokines, particularly those that affect the immune system, people with lung disease, cardiovascular system disorders, neurological disorders, or gastrointestinal problems can be comparatively more affected by COVID-19, resulting in greater mortality rates than in the healthy population.<sup>10</sup> To date, an evaluation and study of the relationship between apical periodontitis and COVID-19 have not been published. It is obvious that diseases increasing cytokine expression in the blood can negatively affect COVID-19 outcomes.

There is a possibility of cytokine storm during COVID-19, and the already existing elevated cytokine levels in apical periodontitis might increase the risk and lead to severe systemic effects on entire systems. In conclusion, the demonstrated increase in serum cytokine expression from apical periodontitis can pose a risk for those with COVID-19, and people with this disorder should be treated preferentially. ■

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