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# Oral and systemic health: An inextricable linkage

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The oral cavity is the linkage between medicine and dentistry and can be considered as the window into the overall health of a patient. The possible link between oral diseases and various systemic conditions has been a matter of interest since years with the issue of causation versus association being widely discussed.<sup>1,2</sup> Several systemic diseases and medications have direct or indirect oral manifestations<sup>3,4</sup> while oral diseases as well have a greater systemic impact.<sup>1,4-6</sup> The association between periodontitis and systemic diseases and conditions including diabetes,<sup>7,8</sup> cardiovascular diseases,<sup>9</sup> adverse pregnancy outcomes,<sup>5</sup> bacterial pneumonia,<sup>10,11</sup> arthritis,<sup>12</sup> neurological disorders<sup>13,14</sup> have been reported in a number of observational and interventional studies.

In recent years, a markedly enhanced understanding of the etiology and pathogenesis of periodontal diseases and associated systemic diseases permits an assessment of the biological plausibility of their putative interactions. The ulcerated sulcular epithelium, in periodontitis, acts as portal of entry for the oral microorganisms, their by-products and pro-inflammatory cytokines to enter the connective tissue and gain access into systemic circulation thus, contributing to chronic systemic conditions and infectious diseases.<sup>4</sup>

A bidirectional interrelationship exists between diabetes and periodontitis. Hyperglycemic state has negative impact on periodontal health and conversely, periodontitis can also adversely affect glycemic control. The diabetic patients have three times greater risk of developing periodontitis than the patients without diabetes. A recent scientific consensus reveals how these widespread chronic conditions reinforce each other and meticulous management of one may assist the treatment of other.<sup>15</sup> Recent studies have shown that chronic inflammation, metastatic infection, and vascular injury from endotoxins are possible oral cavity-based etiologies of cardiovascular diseases.<sup>9</sup> The chronic inflammatory state leads to production of various proinflammatory cytokines, which, along with bacteremia, are believed to initiate atherogenesis and also predispose to the endothelial injury (a precursor to atherogenesis). *Porphyromonas gingivalis*, a potential periodontal pathogen, has also been recognised as a potent agent causing vascular and atherosclerotic changes in cardiovascular disease.<sup>16</sup> Moreover, during dental procedure, streptococci viridans can induce platelet aggregation and cause thrombus formation. Atherosclerotic cerebrovascular disease can further lead to cerebrovascular accidents (strokes) and transient ischemic attacks.

An established association exists between periodontitis and pregnancy-associated oral dysbiosis. Adverse pregnancy outcomes like preterm or low-birth-weight infants are the common obstetric complications of periodontal diseases. The pregnant females with periodontal disease have 7.5 times greater risk of developing this complication.<sup>5,17</sup> Therefore, it would be advisable for the females who are planning pregnancy, particularly those with known periodontal disease to have a thorough periodontal examination and the required treatment. Similarly, the data on the causality and association between oral health and pulmonary infections is debatable

but is shifting to a positive unidirectional relationship.<sup>18</sup> Few studies have demonstrated that the ventilated patients had a positive effect on their systemic health on improving their oral hygiene.<sup>19</sup> Recently, a study done in Korea showed a statistically significant association between periodontitis and radiographic signs of knee osteoarthritis. Similarly, the probability of having osteoarthritis increased along with the increased severity of periodontitis.<sup>12</sup> A recent study have also shown that potent periodontal pathogens, mainly *Porphyromonas gingivalis*, have been linked to the development of dementia; traces of this bacterium have been found in brain tissue of patients who died with Alzheimer's disease.<sup>20</sup> *Porphyromonas gingivalis* and its metabolites gingipains have been detected in brain tissue of Alzheimer patients<sup>13,14</sup> Periodontitis, being a highly prevalent chronic inflammatory disease, might upregulate pro-inflammatory mediators and cytokines that can accelerate the cerebral inflammatory stage, thus affecting pathogenic pathways leading to Alzheimer's disease.<sup>10</sup>

Recently, a possible association between periodontal diseases and increased risk of COVID-19 complications has also been reported.<sup>21</sup> The epithelial cells of oral mucosa and fibroblasts of periodontal ligament show the expression of angiotensin converting enzyme-2 (ACE-2) receptors. These receptors are hypothesized to be the main portal of entry for the viruses into the host cells. Similarly, the presence of SARS-CoV-2 ARS has recently been demonstrated in the gingival crevicular fluid.<sup>22</sup> These probable associations between periodontitis and COVID-19 complications could be attributable to direct effect of periodontitis on systemic inflammation, from an indirect effect of periodontitis on other risk factors of COVID-19, or due to predisposing conditions mutual to both periodontitis and COVID-19.

The concept that oral and systemic health have inextricable connection has been long established yet widely debated. Hence, it is probably safe to presume that there exists an irrefutable association between these two entities. Modification of the co-existing condition may prevent a significant, possibly life-threatening medical outcomes.<sup>4</sup> Hence, from a primary care standpoint, we need a close collaboration between physicians and dentists and should provide a more targeted and specific health education regarding the association between oral and systemic health. If our body gets it, why don't we?

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