

Most Common Dental Complications in Chronic Disease Patients

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Abstract

The term "oral health" describes the conditions of the teeth, gums, and overall oral-facial system, which enables people to chew, speak, and smile. Some of the most common oral disorders are cavities (tooth decay), gum disease (periodontitis), and oral cancer. In the past year, about 40% of people stated feeling oral pain, and by the time they reach 34 years, more than 80% of individuals will have suffered from at least one cavity. External factors that affect the host immunity and systemic health condition may cause dental complications so, in our article we are putting our hands to explore the most common dental complications in chronic diseases patients.

Keywords: Dental; complication; chronic; disease.

1. Introduction

The term "oral health" describes the conditions of the teeth, gums, and overall oral-facial system, which enables people to chew, speak, and smile. Some of the most common oral disorders are cavities (tooth decay), gum disease (periodontitis), and oral cancer. In the past year, about 40% of people stated feeling oral pain, and by the time they reach 34 years, more than 80% of individuals will have suffered from at least one cavity. Annually, the United States spends more than \$124 billion on costs related to dental disorders. Dental emergencies needing emergency care cost more than \$45 billion in missed efficiency and over 34 million school hours on average [1]. Although people often separate oral disorders from other chronic conditions, they are correlated. Other chronic conditions like diabetes and heart disease are related to poor dental health.

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Predisposing habits, including smoking and consuming sugary foods and drinks, may also cause oral illness. Most dental diseases and disorders share preventable risk factors with the four most common terminal conditions: cardiovascular disease, cancer, chronic respiratory disease, and diabetes [2].

Cancer patients undergoing radiation therapy to the head and neck may have short-term and irreversible sensory injuries and acute and chronic soft tissue changes. Besides, radiotherapy reduces the chances of developing osteoradionecrosis and causes poor oral and periodontal health. Mucositis, thick discharges, mucosal contaminations, pain, and sensory disorders are some of the mild side effects of radiotherapy. Chronic effects of head and neck radiotherapy are tissue fibrosis, injury of the salivary glands, increased susceptibility to mucosal illnesses, neuropathic pain, sensory disorders, and a heightened risk of dental caries and periodontal disease [3-5]. Most patients getting radiotherapy for head and neck carcinoma get oral mucositis, an acute response to treatment. Oral mucositis begins as an erythema of the oral mucosa. It progresses to an ulcer and pseudo membranes as the radiation dose continues in those undergoing a standard 6-7 week radiotherapy. Nonkeratinized oral tissues, including buccal mucosa, lateral tongue, soft palate, and floor of the mouth, are more vulnerable to oral mucositis than keratinized oral tissues, even though the anatomical pattern of mucositis mostly correlates with the spread of radiation dose [3-5]. Oral mucositis may be more severe, manifest earlier when being treated, and last longer in head and neck malignancy patients receiving simultaneous chemotherapy and radiotherapy.

The incidences of oropharyngeal candidiasis are also high in patients with head and neck cancer. Apart from oropharyngeal symptoms, oral ingestion can negatively affect nutritional status and capacity to take oral drugs. Oropharyngeal candidiasis causes mucosal pain and taste changes and can spread to the esophagus resulting in dysphagia. Myelo- or immune-suppressed patients may experience regional extension or systemic spread. Clinical manifestations are pseudomembranous (thrush), erythematous candidiasis, and angular cheilitis. Invasive candidiasis and hyperplastic (nodular) candidiasis are rare and may need a biopsy for diagnosis. Further, patients receiving active cancer treatment may experience mucosal pain that affects nutrition and quality of life. Secondary infections with or without dry mouth may result in mucosal pain due to inflammatory response, ulcers, mucosal degeneration, mucosal neuropathy, or mucosal atrophy [3, 4, 5]. Among the potential causes of "radiation-induced" neuropathies are ischemia, neurotoxicity, oxidative stress, and inflammation. Neuropathic signs can start to appear during cancer treatment or later. Mucosal sensitivity is prevalent at one-year follow-up and documented in up to two-thirds of patients. It may remain for a long time after clinical mucositis clears up.

Following radiotherapy, patients are more likely to develop dental caries due to hyposalivation. Saliva is essential in preserving tooth structure because of its impact on pH regulation, antibacterial defense, and tooth cleaning. Dental caries occurs due to a lack of balance in the "demineralization-remineralization" cycle of the tooth resulting in mineral loss and cavitation. Initially, calcification manifests as an upsurge in white lesions along the gum line and the tips of the teeth. Early detection of mineral loss is crucial because untreated caries can spread quickly and require intensive treatment. Its sequel includes pain, jawbone infection, tooth extraction, and the risk of osteoradionecrosis in patients who undertook higher doses of radiotherapy. Irradiated areas may be affected by many structures because of late effects from head and neck cancer radiotherapy [3, 4, 5]. For

instance, radiotherapy to the neck may harm the muscles, nerves, and blood vessels. Injury to the lymphatics may then cause lymphedema, which removes fluid from the head and neck. Fibrosis in the lingual muscles and the constrictor muscles of the pharynx may develop after treatment, which may impair swallowing and tongue function, respectively [6,7]. Masticatory muscle fibrosis may eventually cause trismus, particularly in the lateral pterygoids.

People with either type 1 or type 2 diabetes mellitus are vulnerable to various oral complications. Some complications are geographic tongue, periodontal diseases, oral candidiasis, tooth loss, xerostomia, halitosis, delayed wound healing, burning mouth condition, salivary and taste problems, tooth decay, lichen planus, and dental implant-related disorders. The amount of metabolic regulation and the duration of diabetes affects the degree of periodontal tissue degradation. Diabetes mellitus is a predisposing factor for periodontal disease and influences its frequency and occurrence [8]. Individuals with poorly controlled diabetes often develop deep pockets and attachment loss. Periodontitis affects about 34% to 68% of diabetic patients, with those with poorly controlled diabetes at higher risk of losing their alveolar bones than healthy people. Oral candidiasis is among the early, non-specific indications of unmanaged diabetes mellitus in one-quarter of diabetic people. Candida is a typical oral flora, but in diabetics, hyperglycemia, immunological failure, and acid production make candida infection more likely. Moreover, elevated salivary sugar levels in diabetes patients can promote candida growth and raise the risk of developing oral candidiasis. Most of the types of Candida albicans found in dental plaque are responsible for oral infections.

Patients with diabetes often lose their teeth. According to a recent cross-sectional study, there is a connection between older age and diabetes retinopathy with tooth loss, with 15.3% of diabetic patients losing all of their teeth and only 6.4% keeping all of their natural teeth. Compared to people without diabetes, diabetic patients had 1.46 times the likelihood of having one tooth extracted. The severity of periodontal disease, which causes the breakdown of alveolar bone and ultimately results in tooth removal, is associated with increasing tooth loss in diabetic patients. Periodontal disease-related tooth loss may be due to smoking and bruxism. Further, studies have associated xerostomia's etiology with diabetes mellitus, and it can damage oral functions and compromise a patient's welfare. About 92.5% of diabetes patients (aged 65 to 91) had decreased salivary flow [9]. According to a meta-analysis of 32 trials, 46.09% of diabetic patients had xerostomia, and their salivary flow rates were lower than those of the general population. Salivary secretions are essential for maintaining oral health because they help with mechanical cleaning and support protective actions via biological and biochemical methods [10]. Hyposalivation can impair a patient's ability to eat, maintain a healthy diet, speak clearly, and tolerate dental prosthetics, all of which have an adverse effect on the patient's quality of life. Moreover, it may increase a patient's vulnerability to dental caries, periodontal disease, tooth loss, and the risk of oral infections like candidiasis.

Halitosis is the second most prevalent oral problem among diabetic patients, affecting 52% of individuals. Amongst patients with uncontrolled diabetes, the frequency increased to 76%. However, about 16% of diabetic patients had halitosis. Compared to non-diabetic individuals, diabetic patients with chronic periodontitis had a considerably higher concentration of odoriferous microbes in the tongue covering and sub-gingival plaque [11-13]. Diabetes can as well cause an oral disorder called geographic tongue. The lesion, which affects more men

than women, is located on the dorsum and borders of the tongue and causes pain, uneasiness, and burning feelings [14]. The threadlike papillae degenerate, leaving an erythematous area with an elevated white, yellow, or dimly grey surrounding zone and an ill-defined prickly tongue structure.

More risk factors for oral and dental disease are present in people with mental illnesses than in the general population. The adverse effects of the medications they take, a lack of self-care, challenges in accessing healthcare services, bad attitudes toward healthcare professionals, and patients refusing to cooperate with dental procedures are the leading causes of dental disorders. Dementia, schizophrenia, anxiety disorders, bipolar disorder, and dementia are the most prevalent psychiatric conditions in the community. The fundamental problem with conditions like anxiety and depression is losing interest in self-care, which leads to poor hygiene. Dental cavities and periodontal disease are individuals' most prevalent oral and dental illnesses. Patients with depression frequently have gingivitis, xerostomia, oral candidiasis, oral lesions, and temporomandibular abnormalities. In general, antidepressant medicine is to blame for these findings, particularly xerostomia. In order to prevent such consequences, dentists must educate these patients about how to avoid these problems. When oral candidiasis is present, experts should suggest that patients use artificial saliva, mouthwash, topical fluoride, and other treatments.

Anxiety disorder includes a wide range of subjective and objective indications. It presents with an elevated state of alertness linked to central nervous system excitation manifestations, which would occur in the presence or anticipation of an objective risk, even in the absence of that danger. Dental cavities, periapical, gingival, periodontal, and pulp lesions, and oral cellulitis or abscesses, are the primary disorders these patients exhibit. Besides, people with anxiety experience poor oral hygiene due to losing interest and changing habits and behaviors [15]. Similarly, smoking raises the chance of developing dental cavities because it alters saliva's ability to act as a buffer.

Schizophrenia is a persistent, serious, and disabling condition. According to a study of schizophrenia patients, 61% of people with schizophrenia had poor oral hygiene, which can lead to issues like dry mouth, tooth loss, and severe dental cavities. The side effects of the psychiatric medication these individuals take to explain the dry mouth. Schizophrenia patients should be in a high-risk category for dental disease development. The periodontal disease that these people have is linked to subclinical atherosclerosis, which raises the possibility that cardiovascular disease will manifest in them. Low levels of oral hygiene, fewer dental appointments, smoking, and poor nutrition are additional variables affecting the patients' dental health. The mood swings associated with bipolar disorder can range from manic episodes to sadness and occasionally come on quickly [15]. These patients are more likely to experience bruxism, xerostomia, altered flavor perception, and dental caries. Understanding the various interactions between the medications these people use to treat their disorders is critical.

Dementia is a syndrome marked by a gradual loss of memory, confusion, and issues with cognitive abilities. Alzheimer's, vascular dementia, and dementia with Lewy bodies are a few of the illnesses that might cause it. People with dementia have worse oral and dental health than the general population, more cavities occur in these patients, and their salivation flow is decreased. Dementia patients may not recognize or report pain or discomfort. However, certain behaviors, such as a refusal to eat, persistent face-beating, increased salivation, increased restlessness, and moaning or shouting, can indicate irritation. Dental healthcare professionals should be aware of these symptoms and inform patients' caregivers to seek medical care. The habit of grinding one's teeth together with involuntary, non-functional activities that can happen while awake or sleeping is known as bruxism [15]. The disorders can cause dental wear, mandibular pain, migraines, and, in the most severe cases, speech and swallowing problems. Peripheral, central, and psychological variables, including sleep disturbances, stress, anxiety, depression, and other dental illnesses, affect the pathogenesis of bruxism.

There is solid epidemiological proof that periodontitis increases the risk of developing cardiovascular disease [16-18]. Moreover, it was found that even though in vitro, animal, and clinical research provide evidence for interactions and biological factors, well-designed management trials to examine the effect of periodontal therapy on the mitigation of atherosclerotic heart disease must still be conducted. Some microorganisms can establish an inflammatory environment and lead to a chronic infection in the vessel wall. In contrast, the condition may also trigger an autoimmune reaction against vascular cells, resulting in the atherosclerotic process. In this context, a higher risk of cardiovascular disease is linked to chronic periodontitis and its chronic inflammatory nature [19]. Bacteremia and a systemic inflammation brought on by chronic periodontitis play critical roles in both the beginning of the endothelium lesion and the intensification of the inflammatory process in the vascular wall. Pro-inflammatory cytokines, including TNF-, IL-1, and IL-6, affect the inflammatory reaction in chronic periodontitis and cardiovascular disorders.

There is mounting evidence that chronic obstructive pulmonary disease and periodontal disease are related. Dental biofilm may cause the transport of cytokines and enzymes from periodontally swollen tissues into the lungs, where they may drive local inflammatory reactions before pathogen invasion. Chronic bronchitis, emphysema, and other disorders in the COPD family cause a pathological airflow restrictions in the airways. Smoking, aging, and low socioeconomic status are risk factors for chronic periodontitis and COPD. Moreover, although extensive potential epidemiological research is required, several investigations suggested a link between chronic periodontitis and COPD [20]. Shared pro-inflammatory mediators between COPD and chronic periodontitis may aid in advancing both diseases. Periodontal therapy may enhance lung function and lessen the incidence of COPD exacerbations in COPD patients with chronic periodontitis.

Chronic inflammation is a sophisticated biological process that results in tissue injury in reaction to contagion and other predisposing factors. Dysbiosis of the oral flora and pro-inflammatory processes involving cells and mediators from innate and adaptive immunology are two features of chronic periodontitis. These conditions result in periodontal soft and hard tissues experiencing chronic inflammation, which shares many characteristics with other chronic inflammatory illnesses. Deregulated relationships between innate and adaptive immune systems that cause persistent inflammation in periodontal tissues are the hallmark of chronic periodontitis [20, 21]. The periodontal epithelium is located where the body's internal connective tissue meets its external environment, similar to other mucosal interfaces. Notably, the leading external cause of chronic periodontitis is the existence of dysbiotic microbial populations with the capacity to cause harmful inflammation. However, smoking is a significant factor underpinning the pathogenesis of periodontitis and its impact on the gingival microbiota. Further, additional environmental stresses, including chemical and mechanical ones that exacerbate or encourage mouth inflammation, may influence the onset of chronic periodontitis [22]. However, there is a need for future research to find other pertinent etiological aspects because this is still a relatively untapped field of study. Host genetic variables inside the epithelial lining may contribute to or protect against disease.

External factors that affect the host immunity and systemic health condition may cause chronic periodontitis. Generally, pro-inflammatory host and external factors support a persistent state of inflammation in the periodontal tissues, which can cause damage and eventually result in bone resorption and tooth loss [23]. Thus, studies recognize chronic periodontitis as a chronic non-communicable disease that shares epidemiologic relationships and associated pathological processes with other systemic inflammatory conditions. Chronic periodontitis manifests with persistent inflammation of the periodontal tissues. Treatment plans based on cytokines may help chronic periodontitis and overall health [24-26]. However, considering the intricacy of cytokine systems, it is essential to look at their function in developing chronic periodontitis. Oral microbes and inflammatory activators, which can initiate and support processes involved with the growth of chronic systemic diseases and chronic periodontitis [28,29]. Many systemic diseases (such as rheumatoid arthritis, renal disorders, and neurodegenerative diseases) correlate with chronic periodontitis [30].

In conclusion, diabetes, a compromised immune system, poor oral hygiene, and inheritance are a few chronic illnesses that raise a person's risk for periodontal disease. Gum disease has tobacco usage as a major risk factor. Most patients getting radiotherapy for head and neck carcinoma get oral mucositis, an acute response to treatment. Besides, more risk factors for oral and dental disease are present in people with mental illnesses than in the general population. The adverse effects of the medications they take a lack of self-care. Studies recognize chronic periodontitis as a chronic non-communicable disease that shares epidemiologic relationships and associated pathological processes with other systemic inflammatory conditions. Chronic periodontitis manifests with persistent inflammation of the periodontal tissues. There is rising proof that periodontal disease correlates with chronic obstructive pulmonary disease. Chronic inflammation is a complex biological process that, in response to infection and other risk factors, causes tissue injury. A chronic state of inflammation in the periodontal tissues is typically supported by pro-inflammatory host and environmental stimuli, which can harm the tissues and eventually lead to bone resorption and tooth loss.

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2. Disclosure and conflicts of interest

References

[1]. National Center for Chronic Disease Prevention and Health PromotionCenters for Disease Control and Prevention. "Oral health conditions." Internet: https://www.cdc.gov/oralhealth/conditions/index.html, 2022 2022 2022 162022]. Π. [cited Nov. 16. Available from: Apr. 6. https://www.cdc.gov/oralhealth/conditions/index.html

- [2]. World Health Organization. "Oral health." Internet: https://www.who.int/news-room/factsheets/detail/oral-health, Nov. 18, 2022 [Nov. 16, 2022].
- [3]. H.Y. Sroussi, J.B. Epstein, R.J. Bensadoun, D.P. Saunders, R.V. Lalla, C.A. Migliorati, N. Heaivilin, and Z.S. Zumsteg. (2017, Dec.). "Common oral complications of head and neck cancer radiation therapy: Mucositis, infections, saliva change, fibrosis, sensory dysfunctions, dental caries, periodontal disease, and osteoradionecrosis." *Cancer Medicine*. [On-line]. 6(12), pp. 2918-31. Available at: https://doi.org/10.1002/cam4.1221 [date accessed].
- [4]. K. Onseng, N.P. Johns, T. Khuayjarernpanishk, S. Subongkot, A. Priprem, C. Hurst and J. Johns. (2017, Dec.). "Beneficial effects of adjuvant melatonin in minimizing oral mucositis complications in head and neck cancer patients receiving concurrent chemoradiation." *The Journal of Alternative and Complementary Medicine*. [On-line]. 23(12), pp. 957-63. https://doi.org/10.1089/acm.2017.0081 [date accessed].
- [5]. A. Vesty, K. Gear, K. Biswas, B.W. Mackenzie, M.W. Taylor and R.G. Douglas. (2020, Jun.). "Oral microbial influences on oral mucositis during radiotherapy treatment of head and neck cancer." *Supportive Care in Cancer*. [On-line]. 28(6), pp. 2683-91. https://doi.org/10.1007/s00520-019-05084-6 [date accessed].
- [6]. M.M. Curi, A.F. Condezo, K.D. Ribeiro C.L. Cardoso. (2018, Jun.). "The long-term success of dental implants in patients with head and neck cancer after radiation therapy." *International Journal of Oral and Maxillofacial Surgery*. [On-line]. 47(6), pp. 783-8. https://doi.org/10.1016/j.ijom.2018.01.012 [date accessed].
- [7]. R.V. Lalla, N. Treister, T. Sollecito, B. Schmidt, L.L. Patton, K. Mohammadi, J.S. Hodges, M.T. Brennan and OraRad Study Group. (2017, Nov.). "Oral complications at 6 months after radiation therapy for head and neck cancer." *Oral Diseases*. [On-line]. 23(8), pp. 1134-43.https://doi.org/10.1111/odi.12710 [date accessed].
- [8]. M.J. Verhulst, B.G. Loos, V.E. Gerdes and W.J. Teeuw. (2019, Feb.). "Evaluating all potential oral complications of diabetes mellitus." *Frontiers in Endocrinology*. [On-line]. 10, pp. 56. https://doi.org/10.3389/fendo.2019.00056 [date accessed].
- [9]. M.A. Nazir, L. AlGhamdi, M. AlKadi, N. AlBeajan, L. AlRashoudi-and .M. AlHussan. (2018, Aug.).
 "The burden of diabetes, its oral complications, and their prevention and management." *Macedonian Journal of Medical Sciences*. [On-line]. 6(8), pp. 1545-53. https://doi.org/10.3889/oamjms.2018.294 [date accessed].
- [10]. L. Ferizi, F. Dragidella, L. Spahiu, A. Begzati and V. Kotori. (2018, Oct.) "The influence of type 1 diabetes mellitus on dental caries and salivary composition." *International Journal of Dentistry*. [Online]. 2018, pp. 5780916. https://doi.org/10.1155/2018/5780916 [date accessed].
- [11]. I.L. Chapple, P. Bouchard, M.G. Cagetti, G. Campus, M.C. Carra, F. Cocco. L. Nibali, P. Hujoel, M.L. Laine, P. Lingström-and D.J. Manton. (2017, Mar.). "Interaction of lifestyle, behavior or systemic diseases with dental caries and periodontal diseases: consensus report of group 2 of the joint EFP/ORCA workshop on the boundaries between caries and periodontal diseases." *Journal of Clinical Periodontology*. [On-line]. 44, pp. S39-51. https://doi.org/10.1111/jcpe.12685 [date accessed].
- [12]. N.S. Gasner- and R.S. Schure. (2022, August 16). Periodontal Disease. [On-line].-StatPearls Publishing. Available: https://www.ncbi.nlm.nih.gov/books/NBK554590/ [date accessed].
- [13]. E. Könönen, M. Gursoy- and U.K. Gursoy. (2019, Jul.). "Periodontitis: A multifaceted disease of tooth-

supporting tissues." *Journal of Clinical Medicine*. [On-line]. 8(8), pp. 1135. https://doi.org/10.3390/jcm8081135 [date accessed].

- [14]. M. Sanz, A. Ceriello, M. Buysschaert, I. Chapple, R.T. Demmer, F. Graziani, D. Herrera, S. Jepsen, L. Lione, P. Madianos- and M. Mathur. (2018, Mar.). "Scientific evidence on the links between periodontal diseases and diabetes: Consensus report and guidelines of the joint workshop on periodontal diseases and diabetes by the International Diabetes Federation and the European Federation of Periodontology." *Diabetes Research and Clinical Practice*. [On-line]. 137, pp. 231-41. https://doi.org/10.1016/j.diabres.2017.12.001 [date accessed].
- [15]. J. Torales, I. Barrios and I. González. (2017, Sep.). "Oral and dental health issues in people with mental disorders." *Medwave*. [On-line]. 17(8), pp. e7045. https://doi.org/10.5867/medwave.2017.08.7045
 [date accessed].
- [16]. E.M. Cardoso, C. Reis and M.C. Manzanares-Céspedes. (2018, Jan.). "Chronic periodontitis, inflammatory cytokines, and interrelationship with other chronic diseases." *Postgraduate Medicine*. [On-line]. 130(1), pp. 98-104. https://doi.org/10.1080/00325481.2018.1396876 [date accessed].
- [17]. P.I. Eke, G.O. Thornton-Evans, L. Wei, W.S. Borgnakke, B.A. Dye and R.J. Genco. (2018, Jul.).
 "Periodontitis in US adults: national health and nutrition examination survey 2009-2014." *The Journal of the American Dental Association*. [On-line]. 149(7), pp. 576-88. https://doi.org/10.1016/j.adaj.2018.04.023 [date accessed].
- [18]. F.Q. Bui, C.L. Almeida-da-Silva, B. Huynh, A. Trinh, J. Liu, J. Woodward, H. Asadi-and- D.M.Ojcius. (2019, Feb.). "Association between periodontal pathogens and systemic disease." *Biomedical Journal*. [On-line]. 42(1), pp. 27-35. https://doi.org/10.1016/j.bj.2018.12.001 [date accessed].
- [19]. C. Dörfer. C. Benz, J. Aida and G. Campard. (2017, Oct.). "The relationship of oral health with general health and NCDs: A brief review." International Dental Journal. [On-line]. 67, pp. 14-8. https://doi.org/10.1111/idj.12360 [date accessed].
- [20]. S. Hobbins. I.L. Chapple, E. Sapey- and R.A. Stockley. (2017, May.). "Is periodontitis a comorbidity of COPD, or can associations be explained by shared risk factors/behaviors?" *International Journal of Chronic Obstructive Pulmonary Disease*. [On-line]. 12, pp. 1339. https://doi.org/10.2147/COPD.S127802 [date accessed].
- [21]. A. Lopez-de-Andres, L. Vazquez-Vazquez, M.A. Martinez-Huedo, V. Hernández-Barrera, I. Jimenez-Trujillo, M.A. Tapias-Ledesma, J. de Miguel-Diez and R. Jimenez-Garcia. (2018, Oct.). "Is COPD associated with periodontal disease? A population-based study in Spain." *International Journal of Chronic Obstructive Pulmonary Disease*. [On-line]. 13, pp. 3435. https://doi.org/10.2147/COPD.S174898 [date accessed].
- [22]. A.K. Baldomero, M. Siddiqui, C.Y. Lo, A. Petersen, A.A. Pragman, J.E. Connett, K.M. Kunisaki and C.H. Wendt. (2019, Apr.). "The relationship between oral health and COPD exacerbations." *International Journal of Chronic Obstructive Pulmonary Disease*. [On-line]. 14, pp. 881. https://doi.org/10.2147/COPD.S194991 [date accessed].
- [23]. M.A. Nazir. (2017, Apr.). "Prevalence of periodontal disease, its association with systemic diseases and prevention." *International Journal of Health Sciences*. [On-line]. 11(2), pp. 72-80. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5426403/ [date accessed].
- [24]. S.F. Kane. "The effects of oral health on systemic health." General Dentistry. vol. 65, pp. 30-4, Nov.

2017.

- [25]. T. Larsen and N.E. -Fiehn. (2017, Apr.). "Dental biofilm infections-an update." *Journal of Pathology, Microbiology and Immunology the APMIS Journal*. [On-line]. 125(4), pp. 376-84. https://doi.org/10.1111/apm.12688 [date accessed].
- [26]. V.P. Mathur and J.K. Dhillon. (2018, Mar.). "Dental caries: A disease that needs attention." *The Indian Journal of Pediatrics*. [On-line]. 85(3), pp. 202-6. https://doi.org/10.1007/s12098-017-2381-6 [date accessed].
- [27]. M.A. Peres, L.M. Macpherson, R.J. Weyant, B. Daly, R. Venturelli, M.R. Mathur, S. List, R.K. Celeste, C.C. Guarnizo-Herreño, C. Kearns and H.Benzian. (2019, Jul.). "Oral diseases: A global public health challenge." *The Lancet*. [On-line]. 394(10194), pp. 249–60. https://doi.org/10.1016/S0140-6736(19)31146-8 [date accessed].
- [28]. L.J. Wilkins, M. Monga and A.W. Miller. (2019, Sep.). "Defining dysbiosis for a cluster of chronic diseases." *Scientific Reports*. [On-line]. 9(1), pp. 1-10. https://doi.org/10.1038/s41598-019-49452-y [date accessed].
- [29]. Y. Zhang, X. Wang, H. Li, C. Ni, Z. Du and F. Yan. (2018, Mar.). "Human oral microbiota and its modulation for oral health." *Biomedicine & Pharmacotherapy*. [On-line]. 99, pp. 883-93. https://doi.org/10.1016/j.biopha.2018.01.146 [date accessed].
- [30]. Q. Yuan, Q.C. Xiong, M. Gupta, R.M. López-Pintor, X.L. Chen, D. Seriwatanachai, M. Densmore, Y. Man and P. Gong. (2017, Sep.). "Dental implant treatment for renal failure patients on dialysis: a clinical guideline." *International Journal of Oral Science*. [On-line]. 9(3), pp. 125-32. https://doi.org/10.1038/ijos.2017.23 [date accessed].