

The Putative Role of Oral Microbiome in Premature Aging during HIV Infection: What Do We Know?

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Despite improvements in life expectancy, people with HIV (PWH) are at risk of developing HIV-associated comorbidities at a younger age when compared to HIV-uninfected individuals. This premature aging process can be attributed to various factors, such as the prolonged exposure to combination antiretroviral therapy (cART), inflammation, microbial perturbances and oxidative stress. Similarly to the gut, oral dysbiosis occurs in HIV-1 infection, with cART and inflammation playing a crucial role. This gives rise to an enrichment of pathogenic microorganisms that in turn, elicit an immune response tied to chronic inflammation. Consequently, cART exposure, dysbiosis and persistent inflammation in HIV-1 infection have been associated with the production of reactive oxygen species, mitochondrial dysfunction and telomere shortening, which are known hallmarks of aging. Although looking into these factors provides insight into the mechanisms underlying premature aging in PWH, there is still much we do not know about the oral microbiome and its relationship to HIV-1 infection. The objective of this review is to synthesize current evidence to better elucidate the role of the oral microbiome in HIV-1 infection and its contribution to inflammation and oxidative stress. By addressing these gaps, we aim to provide a novel perspective on the premature biological aging process in PWH and ultimately improve overall health in this population.

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Although combination antiretroviral therapy (cART) has improved the morbidity and mortality of people with HIV (PWH), HIV-1 infection continues to affect millions worldwide and predisposes them to various comorbidities. The persistence of the infection, in combination with prolonged exposure to cART, may contribute to the earlier onset of these conditions (1). Predominantly, HIV-associated comorbidities, such as cancer, neurocognitive impairment, cardiovascular disease, metabolic diseases, and immunosenescence, are also associated with aging in the general population (1). Furthermore, the addition of long-term cART often develops irreversible comorbidities such as dysbiosis of the human microbiome, leaky gut, and microbial translocation (2). HIV-1 infection also promotes the persistent inflammation and premature aging process that occurs in these patients, which are linked to several age-related comorbidities (3). Therefore, identifying the underlying mechanism and contributing factors involved in HIV-1 infection and its associated conditions is important for improving long-term health outcomes.

Among the biological pathways implicated in this process is the human microbiome (2). Certain microorganisms have been characterized when evaluating microbial perturbations in PWH caused by the detrimental effects on the immune system and long-term exposure to cART. When evaluating these perturbances, it was found that similar microbial profiles have also been characterized in the gut and oral cavity of PWH despite responding differently to treatment (2, 4). These differences are important in establishing possible contributing factors of senescence and HIV-associated comorbidities. The risk of developing these comorbidities is also increased due

to cART, which has also been identified as a contributor of dysbiosis (5). Dysbiosis is an imbalance in richness and function of the beneficial microorganisms present in the body, and it is common amongst aging populations. In addition, given the inflammatory process of the infection, shortened telomere length, oxidative stress, and mitochondrial dysfunction are common amongst PWH, all of which are recognized hallmarks of aging (6). Although they have been poorly investigated, associations between oxidative stress, mitochondrial dysfunction, and the microbiome have been reported (7). Investigating these interactions, which may synergistically contribute to premature aging, could lead to the development of different therapeutic and preventive strategies for HIV-1 infection, as well as its comorbidities. In this review, we gathered evidence pertaining to the role of the oral microbiome and how its relationship with cART, inflammation and oxidative stress can shed light on the mechanisms of premature aging in PWH.

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Link between Inflammation, Immunosenescence, and Premature Aging in PWH

When compared to HIV-1 uninfected people, PWH have higher morbidity and shorter life span due to the combined effects of HIV-1 infection and lifelong treatment with cART, (1) which increases the risk of several complications, such as cancer, heart, liver, kidney, neurologic, and bone diseases. Some of these complications are commonly observed among elderly individuals in the general population, reflecting premature aging. Even though there is no cure for HIV-1 infection yet, different regimens of cART have been developed to keep HIV-1 replication under control and reduce the HIV-1 viral load under detection levels (1). Some patients may experience partial recovery of immune function and prolonged survival, although persistent inflammation and immune activation may still remain.

Early in the infectious process, persistence of inflammation can be linked to the acute phase of HIV-1, which is a transient illness that occurs in 40% to 90% of infected individuals. This clinical phase is characterized by increased viral load, rapid HIV-1 replication with an absence of immune response, HIV-1 tissue dissemination, and accumulation of reservoir cells. A recent report indicated that HIV-1 infection was associated with the expansion of monocyte and plasmacytoid dendritic cells, along with increased plasma interleukin-6 and soluble CD14 levels, correlating with monocyte activation independent of cART and potentially contributing to sustained inflammation (8).

Inflammation is a key contributor of HIV- and age-associated comorbidities and a driving factor in premature biological aging. As a person becomes older, a process known as “inflammaging” is commonly seen via T-cell activation, immunosenescence, and the promotion of an inflammatory environment, all of which are commonly observed in HIV-1 (9). In both aging and HIV-1, immunosenescence is characterized by an increased proportion of CD28⁻, CD57⁺, and memory CD8⁺ T cells with reduced capacity to produce interleukin-2, increased production of interleukin-6, resistance to apoptosis, and shortened telomeres (9). This further elucidates that in both there is a similar inflammatory and cellular process. Similarly, the contribution of inflammation to the development of these comorbidities is reflected by elevated levels of soluble CD14 and CD163 receptors, which are markers of monocyte and macrophage activation and microbial translocation. Both are important components of inflammatory signals that bind to lipopolysaccharides and Toll-Like Receptor 4 and are elevated in other age-associated diseases, such as Hepatitis, Rheumatoid Arthritis, and Systemic Lupus Erythematosus (3). High levels of cytokines and chemokines have also been consistently observed in cART-treated patients (3). Although the direct contribution of these inflammatory processes to premature aging is yet to be established, it further depicts the persistent inflammation seen in PWH despite treatment.

Due to the combination of virus activation and cART in PWH, oxidative stress and mitochondrial dysfunction trigger abnormal cellular activation and proliferation, which subsequently increases inflammation and accelerates the aging process (9). Our previous study established that HIV-1 infection and certainly other comorbidities, such as drug abuse, can induce significant reactive oxygen species (ROS) in neuronal cells (10). Similarly, it has also

been observed that monocyte activation enhances the production of ROS in HIV-infected cells (7). This relationship has also been studied in the HIV-1 neutrophils lineage. After stimulation with lipopolysaccharides, ROS production in HIV-neutrophils appeared to be dramatically reduced compared to neutrophils from HIV-uninfected subjects (11). This dysfunctionality is regulated by high levels of histone H3 lysine K4 trimethylated and dysregulation of DNA transcription in circulating neutrophils from PWH (11). Even though general factors and processes, such as the ones mentioned above, that lead to chronic/persistent inflammation and aging in HIV-1 infection have been identified, further studies are necessary to establish the direct relationship and contribution of cART and/or HIV-1 infection on inflammation.

Importance of Oral Immune Response in PWH

After the acute HIV-1 infection, the early immune response is an important factor in determining the clinical course of the disease. The primary sites of HIV-1 infection are the vaginal, anal and, more rarely, the oral mucosa. Nonetheless, oral health is still underestimated, especially in underdeveloped countries, and has been poorly investigated in literature. Oral complications in PWH also remain a significant problem given the high incidence of oropharyngeal cancer (12). Indeed, the oral mucosa and secretions, and their relationship with commensal bacteria are key determinants of oral health and immunity.

A high level of mucosal HIV-1 replication is required for virus evasion of innate immune responses, facilitating the exposure to target cells, and establishment of persistent infection (13). The persistence of HIV-1 in mucosal tissue and its replication in immune system cells causes damage to mucosal barriers, leading to microbial barrier translocation and hyper-activation of the immune system (14), hence resulting in higher propensity of colonization by commensal and pathogenic microorganisms. Disruption in this microenvironment contributes to HIV-1 dissemination, oral opportunistic infections, and cancer susceptibility. Cellular innate immune components of the oral cavity are composed primarily of epithelial cells, intraepithelial lymphocytes, fibroblasts, granulocytes, macrophages, dendritic cells, and natural killer cells, which all play a crucial role in oral immunity (15). Elevated levels of cytokines secreted in saliva, such as tumor necrosis factor- α , interleukin-1 β , and interleukin-6, have been seen in PWH, which promotes a chronic, low grade inflammatory state, facilitating HIV-1 infection (16). Furthermore, when compared to PWH, studies have found that HIV-1 uninfected individuals have non-immune endogenous inhibitors of HIV-1, such as secretory leukocyte protease inhibitors (17, 18). These are important given that they help protect adherent monocytes and activated peripheral blood mononuclear cells against HIV-1 infection (17, 18).

Soluble immune factors and cellular innate immune responses control the mucosal integrity and are the first to identify abnormal microorganisms (15). Furthermore, they are constantly modulated by diverse and changeable microbiome communities throughout the lifetime of an individual. They are also dysregulated by host immunity, as is seen with HIV-1 infection. This crosstalk between oral immunity and the existing microbiome is a link to maintaining a controlled oral inflammation. Aside from HIV-1 infection, the

host-immune response is also dysregulated in oral inflammatory diseases, such as periodontitis, which has been suggested to trigger systemic and chronic inflammation (19). In an experimental periodontitis model, the higher CD25+ B cell frequency, interleukin-10, interleukin-35, and Transforming Growth Factor- β production alleviated periodontal inflammation and alveolar bone resorption (20). Hence, investigating the interactions between soluble immune factors, innate immune responses, and microbial perturbances may be crucial for understanding oral inflammation in conditions, such as periodontitis, a common comorbidity of PWH.

Impact of cART on Oral Immunity and Health in PWH

The impact of HIV-1 infection in oral immune response can be associated to the role of cART in oral health. A systematic review reported that oral warts were seen more often in patients receiving cART (13). One of the drugs most widely used in cART, tenofovir, exhibits cellular and molecular alterations in the oral epithelium through the changes in cytokeratin (21). This enhances the inflammatory processes and abnormal epithelial repair and proliferation (15). HIV-1 pre-exposure prophylaxis has been shown to induce an alteration in the inflammatory cytologic response in oral mucosa (22). Increased prevalence of HIV-1 salivary gland disease has also been reported in PWH undergoing cART, which may be associated with an increased risk of carries and gingival inflammation (17, 23, 24). Additionally, no changes in the prevalence of oral candidiasis, aphthous ulcers, oral warts, herpes simplex virus lesions and Kaposi's sarcoma were found with cART (24). Even though early initiation of cART in PWH has been shown to lower the risk, the prevalence of non-AIDS-defining cancers, such as oropharyngeal cancer, have been documented to increase with cART (12). Hence, despite the benefits from this treatment, there are other adverse contributing factors of cART that affect oral health in PWH.

The Microbiome and its Impact on Health and Diseases

In the human body, multiple microorganisms coexist in a symbiotic relationship. These commensal microorganisms, including archaea, bacteria, fungi, viruses, and parasites, are collectively known as microbiota. Their joint genomic information as part of the human microbiome has raised interest in the role they play in health and disease. Our microbiome can enhance our health or positively impact a range of conditions, such as diabetes, obesity, allergies, inflammation, cancer, and cardio-metabolic diseases (25). For example, diet and exercise have been shown to positively enhance the gut microbiome and immune response, presenting as possible preventive strategies for targeting premature aging in PWH (26, 27). Furthermore, it can also modulate the immune system's activity and its relationship with several infectious diseases (25). Particularly, the human microbiome has become an important factor when studying the pathogenesis of HIV-1. It has been well documented that microbial translocation and chronic inflammation are commonly found throughout the course of the disease, but its role in many comorbidities and aging is yet to be investigated (3). Therefore, there is substantial information that remains unknown about the association between the microbiome, aging, and HIV-1, particularly when evaluating the oral microbiome.

HIV-1 Infection, cART and the Oral Microbiome

When evaluating the role of the oral microbiome in HIV-1 and aging, several factors must be taken into consideration, given that they potentially affect or may be affected by the microbial profiles. Some of these factors include cART, oral infections, and inflammation. Dysbiosis normally occurs within the oral microbiome and, given that it is common amongst PWH, has also been established as a hallmark of oral opportunistic infections (5, 28, 29), which in turn have been linked to immune dysfunction (30).

Despite the wide current use of cART, frequently reported diseases include periodontal disease, oral candidiasis, HIV-1 salivary disease, Human Papillomavirus infection and lesions, xerostomia, and ulcerations (5). During periodontal disease, systemic inflammation has been correlated to the growth of pathogenic bacteria, such as *Fusobacteria*, *Prevotella*, and *Porphyromonas spp.* Predominantly, enrichment of Gram-negative bacteria has been observed with increasing periodontal disease severity, which can promote immune activation due to lipopolysaccharides release and their translocation to the systemic circulation (28).

Interest has peaked in *Porphyromonas gingivalis*, a Gram-negative pathogen that had been previously identified as a "keystone pathogen" because of its close association to periodontitis (31). Keystone pathogens are responsible for causing dysbiosis through the modulation and impairment of the host's immune response, even if their population within the oral cavity is not very dense (32). *P. gingivalis* elicits an array of virulence factors that help it thrive in overproportion, including lipopolysaccharides. In the context of periodontitis-causing *P. gingivalis*, the host immune response elicits an extraordinary release of inflammatory molecules by human monocytes through a CD14-dependent mechanism (32).

Changes in Microbial Diversity and Composition

Differences in the pathogenesis of oral infections may be due to different variables, such as changes in the CD4+ T-cell count and cART therapy regimens in HIV-infected individuals (30). Several studies have shown that cART alters the oral microbial composition of PWH (5, 28-30).

Recent data demonstrated that HIV-infected individuals harbored significantly richer bacterial communities compared to the saliva samples from HIV-uninfected individuals (33). Five species of *Spirochaeta* including, *Spirochaetaceae*, *Spirochaeta*, *Treponema*, *Treponema amylovorum*, and *Treponema azotonutricum* were significantly abundant in the saliva of HIV-infected individuals, whereas *Helicobacter* species were significantly reduced (33). Due to their strong proteolytic activity, *Spirochaeta* play a potential role in the development of oral infections, such as gingivitis and periodontitis, and in the disruption of essential functions of host cells and immunoglobulins (34). On the other hand, *Helicobacter pylori* have been frequently found in the oral cavity of PWH undergoing cART, as well as *Acinetobacter baumannii* and *Pseudomonas aeruginosa*, all Gram-negative bacteria that may contribute to oral dysbiosis and inflammation (35). Important changes in bacterial diversity in the saliva of patients with lower CD4+ T cells after 24 weeks of cART were found and it was

concluded that the oral microbiome may be relevant in CD4+ T-cell count recovery after cART (36). Additionally, an assessment of the number of microbial species found showed a reduction on the measured amount of diversity in the bacterial community (Shannon index) and showed the *Firmicutes* and *Prevotella* phyla proliferated after induction of cART (37).

Fungal infections, such as oral candidiasis, remain as one of the most important contributors of dysbiosis in the oral microbiome during HIV-1 infection. Although present in normal conditions as part of the gastrointestinal flora, candidiasis is characterized by the accumulation of *C. albicans*. Evidence has shown that oral *Candida* infection occurred in one-third of subjects with advanced AIDS, even in the setting of cART (38). This persistence suggests that immune reconstitution achieved through cART may not fully restore mucosal immunity, allowing *Candida* to thrive and contribute to ongoing inflammation and epithelial disruption.

Specific effects of cART regimes on Oral Microbiome

Furthermore, evidence suggests that different cART regimens can have different effects on the oral microbiome. For example, nucleoside reverse transcriptase inhibitors have been associated with decreased oral diversity compared to a nucleoside reverse transcriptase inhibitors + Non-nucleoside reverse transcriptase inhibitors regimen (28).

In the gut, changes in microbial diversity due to different cART regimens have been linked to alterations in gastrointestinal functions (2). A study found that conventional nucleoside reverse transcriptase inhibitors-based cART can cause a drastic reduction in *Bacteroides* genus and increase in *Succinivibrio* and/or *Megasphaera* genera, suggesting an association with defects in gastrointestinal function, such as diarrhea and abdominal pain (2). cART has also been shown to increase the risk of recovering certain periodontal pathogenic bacteria such as, *Fusobacterium species*, *Peptostreptococcus micros*, *Campylobacter species*, *Eubacterium species*, and *Tannerella forsythia*, in HIV infected women (39). Higher levels of *Prevotella* have been observed in the oral composition of HIV-infected women undergoing cART compared to those without cART (29). In the gut, *Prevotella* has been shown to enhance mucosal inflammation through Th17 cells, contributing to systemic inflammation; therefore, higher levels of *Prevotella* in the oral microbiome may likewise be a contributing factor to systemic inflammation (4). In addition, Th17 cells have been shown to play a crucial role in maintaining oral barrier integrity in response to damage induced by IL-6 (40). For these reasons, the effects of different cART regimens in the oral microbiome must be considered and may also play a factor in the development of age-associated comorbidities.

Relationship between the Oral Dysbiosis and Aging in PWH

Although oral dysbiosis normally occurs with aging and HIV-1 infection, the role of the human microbiome in the aging process of PWH is not yet fully understood. The advancement of cART has been associated with a direct effect on microbial composition (28). A study comparing the oral microbiome of women found higher proportions of *Actinobacteria* and *Fusobacteria* in aging individuals (>50 years old [y/o]) with and without HIV compared to those of

young adults (<35 y/o), suggesting age related microbial shifts that may influence oral and systemic health (29). Long-term cART has also been linked to abnormal cellular function, homeostasis, and cell activation status, which can, in turn, contribute to premature aging in HIV-1 infection (41). Moreover, higher levels of viral replication, when compared to uninfected adults, promote chronic inflammation and immune activation, leading to high expression of T-cell surface activation markers and CD95 apoptotic markers. Immune dysfunction also causes CD8 T-cell exhaustion and apoptosis due to the incremental loss of proliferative and effector properties (41). Together, these findings highlight the complex interplay between microbial alterations, immune dysregulation, and accelerated aging in PWH.

There are several other mechanisms that should be further studied to understand this relationship. For instance, perturbances in the oral microbiome contribute to an inflammatory environment through the increase of pro-inflammatory bacteria, which in turn can be linked to immune activation/dysregulation (42). For example, higher levels of *Bifidobacterium sp.* are associated with higher levels of soluble tumor necrosis factor receptors 1 and interleukin-6 in PWH, compared with HIV-uninfected individuals (5). Alpha diversity (mean species diversity) from saliva has also been associated with CD4/CD8 ratio (a marker of immune suppression). The same study also established that higher CD4/CD8 ratio is associated with lower morbidity and mortality, and that high levels of plasma HIV-1 RNA levels correlated with low levels of bacterial genera *Lactobacillus* and *Streptococcus* (28). On the other hand, a correlation between the high levels of these genera and high levels of CD4+ T-cell counts have also been established (29). Together, these findings highlight several mechanisms into the role of the oral microbiome as a contributor of inflammation and immune activation, eventually leading to premature aging.

Hallmarks of Aging: Mitochondrial Dysfunction and Telomere Shortening

Associations between HIV-1 infection and hallmarks of aging are essential for understanding the premature biological aging in PWH. HIV-1 infection and cART have been shown to induce mitochondrial dysfunction, which has been established as a hallmark of aging (36). This can be seen through several mechanisms, such as deregulation of ETC respiration and ATP synthesis, mtDNA damage, and increased oxidative stress (6). Furthermore, although a direct mechanism has not been identified yet, increase generation of ROS seen with age has been identified as an important contributing factor in age-related diseases and individual health-span (43, 44).

PWH have been shown to exhibit increased ROS production in monocytes of pro-inflammatory cytokines, which has been linked to increased HIV-1 replication (45). Apart from mitochondrial dysfunction, HIV infection has been associated to shorter telomere length, which is another known hallmark of aging (46). Additionally, correlations between telomere length and poor immunological recovery have been found (46). These findings suggest that mitochondrial dysfunction and telomere length play an important role in the accelerated biological aging and senescence process of PWH (6, 46).

Oxidative Stress as a Mediator Between Oral Health and Aging

Increased oxidative stress and worsened oral health in PWH can be linked through the HIV-associated comorbidities, such as oral cancers, diabetes, rheumatoid arthritis, chronic inflammation and neurodegenerative diseases (47). Additionally, imbalances in the production of ROS and the host's inability to produce sufficient antioxidants to repair the resulting damage contribute to oxidative stress, which has been linked to periodontal disease (48). In patients with periodontitis, the levels of markers of oxidative damage in chronic inflammatory diseases were significantly higher, establishing a relationship between proinflammatory and oxidative stress biomarkers (48). In addition, lower CD4+ T-cell count has been correlated with increased HIV-1 viral load, further contributing to more severe oxidative stress (7).

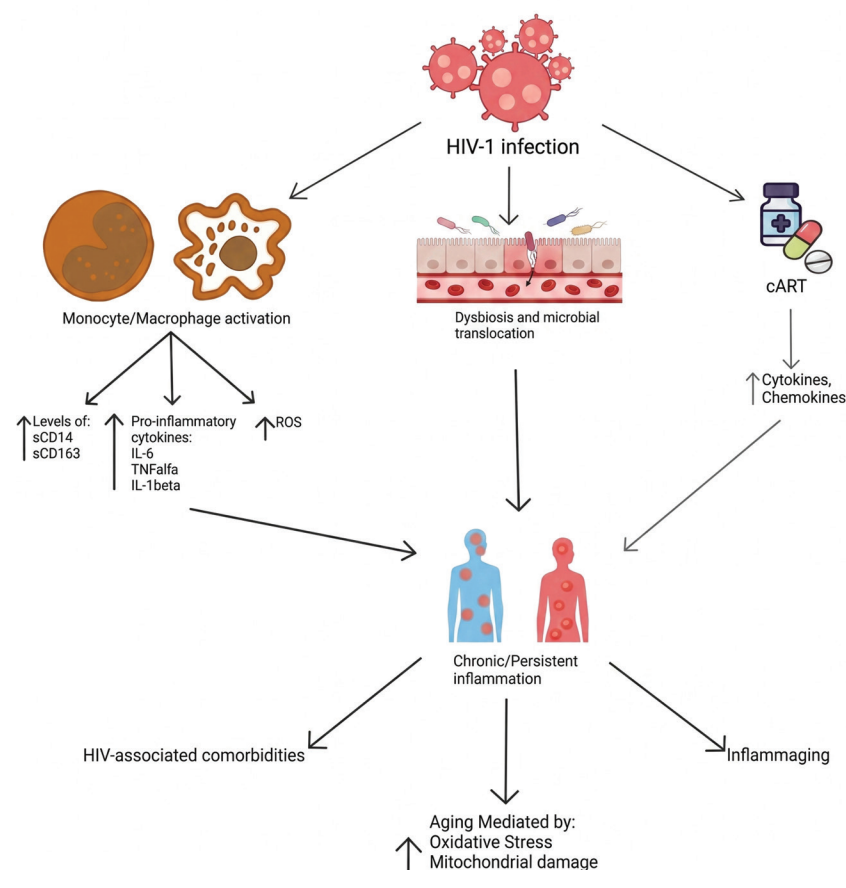
The gut microbiome has been linked to the production of ROS (49). For example, a decrease in healthy microbial members, such as short-chain fatty acid producers and anaerobic fermenters, and an increase in opportunistic bacteria, such as Gram-negative bacteria, facilitate the production of ROS, enhancing oxidative stress (49). Even though it has been poorly investigated, the relationship between microbial composition and oxidative stress in the gut gives us a notion of the potential role of these factors within the oral microbiome. Few associations have been established that provide a relationship between the oral microbiome and oxidative stress. Salivary markers such as Thio barbituric acid reacting substances, advanced glycation end products, advanced oxidation protein products, total antioxidant capacity, and ferric reducing ability of saliva have been useful in oral diseases, such as periodontitis, to detect oxidative stress (50). A particular study also aimed to identify how differential taxa correlates with levels of oxidative stress. Even though the results were not consistent, it showed a significant correlation with *Streptococcus mutans*, which are capable of producing ROS *in-vitro*, and oxidative stress (50). Hence, given the potential role of the oral microbiome in oxidative stress, more studies are needed to evaluate how changes in the oral microbiome promote premature aging in PWH.

Proposed Biological Pathway of Aging

When evaluating possible pathways of biological aging and their outcomes in PWH several factors should be considered. One of these is cART, which is the main

course of treatment for PWH. It has been established that cART plays a role in oral microbial dysbiosis (5, 28, 29). On the other hand, even though it helps reduce the inflammatory response, inflammation remains high among individuals undergoing cART. Changes in the oral composition have also been associated with inflammatory markers and response; hence, dysbiosis can be considered another contributor to an inflammatory environment. Inflammation can also contribute to the production of ROS and oxidative stress, which have been established as hallmarks of aging. As another route of aging in PWH, HIV-1 infection can be considered a direct contributor to aging. This can be seen due to the pathological effects caused by the infection, such as the depletion of the immune cells, immune activation, and chronic inflammation (Figure 1).

Figure 1. HIV-1 and cART contribute to oral dysbiosis and premature aging. Schematic representation of HIV-1 infection-induced oral dysbiosis in PWH that leads to chronic inflammation, which leads to the generation of reactive oxygen species and, furthermore, to neuroinflammation and neurodegeneration. Persistent inflammation in the brain causes significant production of LPS and causes premature aging in the PWH. In addition, the synergistic effect of HIV-1 infection and cART also causes chronic inflammation which contributes to the sequential process as mentioned above. Footnote: Arrows in this figure represent a schematic depiction of causality between variables. Specifically, the arrows indicate the direction of influence or relationship between the elements shown. Arrows pointing upwards next to inflammatory markers and mediators signify an increase in the levels of the variables in the described context.



Conclusion

Although the oral microbiome represents an important target to treat HIV-1 infection and associated comorbidities, it is poorly understood. Similarly to the gut, the oral microbiome is affected by HIV-1 infection. Not only the virus itself, but cART and inflammation, independently and synergistically, play a crucial role in oral microbial dysbiosis and biological aging. These microbial perturbations have also been associated with immune function, given that differences in T-cell activation can be seen when comparing microbial compositions. Aging can be observed in different ways when analyzing the oral microbiome, especially through oxidative stress. Oxidative stress has a direct link with mitochondrial dysfunction, cART, inflammation, and immune activation. Several associations suggest that the microbial composition may also contribute to oxidative stress. Thus, characterizing the oral microbiome and establishing its relationship with inflammation, oxidative stress, and mitochondrial damage presents itself as a novel possible approach of understanding the aging process of PWH and ultimately improve overall health in this population.

Resumen

A pesar de las mejoras en expectativa de vida, las personas con VIH (PCV) siguen en riesgo de desarrollar condiciones relacionadas al virus a una edad más temprana que las personas sin VIH. Este proceso de envejecimiento temprano puede ser causado por varios factores, como la exposición continua al tratamiento de combinaciones antirretrovirales (cTAR), inflamación, perturbaciones en el microbioma y el estrés oxidativo. Al igual que en el intestino, la disbiosis oral se ha visto en la infección por VIH-1, con cART e inflamación desempeñando un rol importante. Esto da lugar al enriquecimiento de microorganismos patológicos que, a su vez, desencadenan una respuesta inmune asociada a la inflamación crónica. En consecuencia, la exposición a cTAR, la disbiosis y la inflamación persistente en la infección por VIH-1 se han relacionado a la producción de especies reactivas de oxígeno, la disfunción mitocondrial y el acortamiento de los telómeros, los cuales son marcadores de envejecimiento. Al estudiar estos factores, aportamos información valiosa sobre los mecanismos que llevan al envejecimiento prematuro en PCV. No obstante, aún queda mucho por conocer acerca del microbioma oral y su relación con el VIH-1. El objetivo de este manuscrito es recopilar la evidencia disponible para entender mejor el papel del microbioma oral en la infección por VIH-1 y su contribución al proceso de inflamación y estrés oxidativo. Al abundar sobre este tema, presentamos una perspectiva novedosa sobre el proceso de envejecimiento biológico prematuro en las PCV con la meta de mejorar la salud general de esta población.

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