Pathogenic Bacteria Associated with Periodontitis

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ABSTRACT: Oral pathogenic bacterial species have a direct impact the pathology of tooth decay and gum disease. Oral pathogenic bacteria engage in negative cooperation with the host by exchanging information, immunological responses, and metabolic status through bidirectional communication between the systemic organs and mouth cavity. The oral cavity serves as a crucial interface between the human body and the surrounding environment. The microbial compositions in different regions of the oral cavity vary due to the distinct microenvironments present. These microenvironments are influenced by a combination of intricate signals, hosts, and external ecological factors. This review highlights the causative bacterial agents that are responsible for adult periodontitis.

INTRODUCTION

The existence of microbial populations is the cause of oral and dental diseases, including periodontal disorders, pericoronitis, gingivitis, endodontitis, peri-implantitis, and post-extraction infections. These infections can be caused by many different types of bacteria. There are distinct clinical and microbiological characteristics that are associated with each of these diseases. The mouth cavity harbors approximately 10^{10} bacterial species, with more than 500 species considered to be regular residents. Nevertheless, a few 150 bacteria species have been identified and grown in laboratory conditions from root canals. Studying the intricate and important microbial communities in many parts of the human body, such as the nasal cavity, oral cavity, intestine, and vagina, is one of the top five research objectives.(Terehi et al, 2018).

The oral microbiome, sometimes referred to as oral microbiota or oral microflora, comprises the bacteria that inhabit the human mouth. The microbiome in question was initially observed by the Dutch scientist Antony van Leeuwenhoek, who utilized a self-designed microscope to make this groundbreaking finding. Van Leeuwenhoek, renowned as the progenitor of microbiology, was a trailblazer in the identification of both protists and bacteria. In 1674, he observed his own tooth plaque and reported observing "microscopic organisms in motion." (Deo & Deshmukh, 2019).

The Human Microbiome Project (HMP) places significant emphasis on studying the oral microbiome. The completion of the Human Microbiome Project (HMP) has greatly enhanced our comprehension of oral microorganisms. This knowledge goes beyond their roles in tooth decay, gum disorders, and other mouth-related problems, offering a more comprehensive understanding of the functions of bacteria in the mouth. (Kilian et al., 2016).

Evidence increasingly supports Miller's oral lesion theory. Periodontitis-induced inflammation results in the destruction of connective tissues and bones, with extensive inflammatory cell infiltration in the connective tissue near the periodontal pocket epithelium. This low-grade inflammation is believed to negatively impact overall health and exacerbate other systemic diseases. Consequently, chronic periodontitis in the general population is considered a significant source of undetectable peripheral inflammation. Thus, periodontitis is often referred to as a "low-grade systemic disease" due to its impact on various systemic conditions. (Gao et al., 2018).

Scientists have recorded different species associated with oral infections. For examples; like *Pepto-streptococcus micros, Eikenella corrodens , Prevotella intermedia, Fusobacterium nucleatum , Eubacterium* specie, *Porphyromonas gingivalis, Actinobacillus actinomycetem-comitans, Campylobacter rectus, , Bacteroides forsythias* .There is a relationship between *Treponema pallidum*-related spirochetes and the acute necrotizing ulcerative gingivitis (ANUG). On the other hand, *Porphyromonas endodontalis* was observed to be particularly correlated to endodontic infections. This species was account for of periodontitis (gum diseases) and caries (tooth decay) that are the two major known oral infections (Yamashita & Takeshita, 2017).

The oral cavity of a healthy periodontium is inhabited by non-pathogenic commensal microorganisms. Under typical circumstances, the indigenous microorganisms present in the mouth stimulate the body's natural defense mechanism in the tissues

Pathogenic Bacteria Associated with Periodontitis

surrounding the teeth, assisting in the control of bacterial growth in the area around the gum line. In this specific microenvironment of the periodontium (Zarco et al., 2012).

PORPHYROMONAS GINGIVALIS

One form of bacterium known as Porphyromonas gingivalis is characterized by its inability to utilize oxygen and its tendency to leave a pink stain when subjected to a certain laboratory test. It is frequently seen in the mouth and has a role in the evolution of periodontitis, which is an inflammatory disease that causes damage to the tissues that support the teeth and can eventually result in the loss of teeth. The oral cavity is home to over 500 different kinds of bacteria. Among these bacteria, the "red complex" that includes Porphyromonas gingivalis, Treponema denticola, and Tannerella forsythia has been found to have a strong correlation with severe periodontal disorders. (Mysak et al., 2014).

Porphyromonas gingivalis, a prominent pathogen in severe gingivitis (a persistent inflammatory condition), is a substantial component of the oral microbiome and a proficient colonizer of the oral epithelium. This bacterium has the ability to infiltrate the gingival tissues in close proximity and successfully avoid the body's defense mechanisms. It employs many virulence factors to alter the body's natural immunological and inflammatory responses. Porphyromonas gingivalis is closely associated with chronic gingivitis, as its ability to remain in the gums relies on its capacity to elude the host's immune system while still allowing some level of inflammatory response. This pro-inflammatory condition is beneficial for this bacterium and other infections that cause periodontal disease. The gingival crevicular fluid, which is an inflammatory discharge, contains important nutrients such as peptides and iron produced from heme. Porphyromonas gingivalis exacerbates severe gingivitis by inducing elevated amounts of pro-inflammatory cytokines, such as IL-1β and IL-6, via peripheral CD4+ T helper cells. (Kinane et al., 2008).

BACTEROIDES FORSYTHUS

Bacteroides forsythus, a form of bacteria that is shaped like a spindle and does not require oxygen to thrive, has been strongly linked to the development of serious gum disease when it is present in the bacteria that dwell below the gum line. This is because the bacteria do not require oxygen to make their lives possible. B. forsythus has been shown to contain a relatively modest number of potential virulence factors, despite the fact that this is evident. This is because of the nature of its development, which requires a great deal of caution, as well as the difficulties that are linked with producing it from the mouth cavity of humans. A trypsin-like protease, a sialidase, a particular protease that is expressed by the prtH gene, and a cell surface-associated protein of B. forsythus that assists in binding to fibronectin and fibrinogen are some of the virulence factors that have been discovered. Another virulence factor is a sialidase. (Hasebe et al., 2004).

PREVOTELLA INTERMEDIA

Prevotella is a genus that belongs to the Bacteroidetes phylum. It consists of rod-shaped bacteria that are Gram-negative and can only survive in the absence of oxygen. These bacteria are commonly found in dental plaque and the gut microbiome. Prevotella intermedia is frequently found in the plaque below the gum line in people with gum disease and is acknowledged as one of the disease-causing microorganisms that contribute to long-lasting inflammation of the gums, known as chronic gingivitis. It is classified as a member of the orange complex group. (Naito et al., 2022).

Furthermore, these bacteria have been linked to a wide variety of oral diseases, including endodontic infections, pregnancy gingivitis, and acute necrotizing ulcerative gingivitis, to name a few conditions. They are also found in extramural locations, such as NOMA lesions (cancrum oris). Previous research has identified several potent virulence factors in P. intermedia, including adhesins, the proteolytic enzyme interpain A, and lipopolysaccharides. Biofilm formation may also play a crucial role in virulence, as studies suggest that bacterial cells within biofilms exhibit greater resistance to antibacterial agents and antibiotics across multiple microorganisms. Additionally, it has been noted that P. intermedia cells within biofilms demonstrate heightened antibiotic resistance. However, the precise mechanisms of virulence employed by P. intermedia remain to be fully understood. (Nagaoka et al. 2014).

FUSOBACTERIUM NUCLEATUM

Fusobacteria are a type of bacteria that are Gram-negative, meaning they do not retain a specific stain during the Gram staining process. They are anaerobic, which means they do not require oxygen to survive. Fusobacteria are rod-shaped and can be found in some areas of the human oral cavity, gastrointestinal system, and other parts of the body. A clear association has been observed between the presence of F. nucleatum and colorectal cancer in several groups of individuals and at different disease stages. F. nucleatum is commonly considered an opportunistic pathogen because it is often found in anaerobic samples taken from patients with different types of illnesses. While this association is recognized by oral and medical microbiologists, it remains a subject of ongoing research and investigation. (Brennan & Garrett, 2019).

Fusobacteria are currently divided into two families: the Leptotrichiaceae family, which includes genera such as Leptotrichia, Sneathia, Sebaldella, and Streptobacillus; and the Fusobacteriaceae family, which includes marine and aquatic genera such as

Pathogenic Bacteria Associated with Periodontitis

Psychrilyobacter, Ilyobacter, Propionigenium, and Cetobacterium, in addition to the animal-associated genus Fusobacterium at the moment. It is not only that F. nucleatum has acquired the power to build connections with the microbial population that is present in the oral cavity, but it has also developed the ability to make strong connections with mammalian cells and tissues that are found in the mouth. Fusobacterium nucleatum is responsible for a number of important and beneficial jobs that take place within biofilms. These tasks have an effect not only on the development of periodontal disorders but also on the overall health of the biofilms themselves. (Hendrickson et al., 2014).

Within a dental plaque biofilm, Fusobacterium nucleatum serves as a bridging organism that links initial colonizers such as Streptococcus species to primarily anaerobic secondary colonizers such as Porphyromonas gingivalis and Aggregatibacter actinomycetemcomitans. This is an extremely important role that Fusobacterium nucleatum plays. Because of its distinctively elongated structure, F. nucleatum is capable of interacting with a wide variety of different microbial cells. Under the conditions of co-cultivation with Streptococcus sanguinis, F. nucleatum and S. sanguinis are capable of producing corncob-shaped formations that are well-structured. These formations are characterized by the attachment of a maximum of ten S. sanguinis cells to a single F. nucleatum cell. Because of this, the elongated cylindrical form of F. nucleatum is essential for the creation of polymicrobial biofilms and microbial interactions because it enables structural linkages that are essential for the establishment of these environments. (Guo et al., 2017).

AGGREGATIBACTER ACTINOMYCETEMCOMITANS

Aggregatibacter actinomycetemcomitans is a type of bacteria that prefers environments with high levels of carbon dioxide and has a coccobacillus shape. It may be identified by its ability to retain a pink stain when subjected to the Gram staining technique, indicating that it is Gram-negative. It is commonly observed in the mouths of teenagers and young adults who have aggressive types of periodontal disease. Localized aggressive periodontitis, often referred to as localized juvenile periodontitis, commonly targets the first permanent molars and incisors in teenagers. (Herbert et al., 2016). Moreover, A. actinomycetemcomitans has been associated with infections outside the oral cavity, including infective endocarditis, bacterial arthritis, septicemia during pregnancy, cerebral abscesses, and osteomyelitis. Nevertheless, the oral cavity is the main origin of these infections, which requires the movement of A. actinomycetemcomitans from the oral cavity to areas outside of the mouth where the infection occurs. (Antony et al., 2009)..

The Virulence factors of *A.actinomycetemcomitans* engage with host cells to trigger an abnormal inflammatory reaction in the gingival tissues of the periodontium. It has been observed that the migration of polymorphonuclear leukocytes (PMNs) across the epithelium into the gingival sulcus leads to the formation of a pseudo-barrier. This barrier consists of several layers of cells and acts as a separation between the plaque and the surface of the junctional/sulcular epithelium. (Herbert et al., 2016).

The initial cellular response is initiated by non-hematopoietic resident cells, such as gingival fibroblasts and epithelial cells.Furthermore, *A.actinomycetemcomitans* possesses virulence factors that consist of both exotoxins and endotoxins. These molecules induce host responses by activating surface epithelial cells and underlying fibroblast cells. *Aggregatibacter* actinomycetemcomitans is capable of efficiently traversing the gingival epithelium.(Fives-Taylor *et al.*, 1999), Once *A. actinomycetemcomitans* successfully overcomes these first barriers, it triggers a host inflammatory response. Once *A. actinomycetemcomitans* infiltrates the deeper layers of the subgingival tissues, it triggers a more extensive immunological response in the host. (Kelk et al., 2011).

PEPTOSTREPTOCOCCUS.

Gram-positive anaerobic cocci (GPAC), commonly referred to as peptococci and peptostreptococci, have been found in various locations within the body. The majority of clinical isolates of GPAC belong to the Peptostreptococcus genus. These bacteria are regarded as indigenous microorganisms that naturally inhabit many regions of the human body, including the mouth cavity, skin, upper respiratory and gastrointestinal tracts, and the female genitourinary system. (Riggio & Lennon, 2003).

There have been a number of oral infections that have been linked to different species of Peptostreptococcus. It has been found that P. micros and P. anaerobius are present in endodontic abscesses. On the other hand, P. magnus, P. anaerobius, P. prevotii, and P. micros have been linked to infections in dental root canals. In addition, Peptostreptococcus species have been linked to the development of gingivitis and periodontitis in human patients. For instance, P. micros has been connected with periodontal injury, particularly in regions that are impacted by active disease. On the other hand, P. anaerobius has been observed to be associated with gingivitis as well as periodontitis. (Capunitan & Conte, 2010).

CONCLUSIONS

The study of the oral microbiome is a dynamic and rapidly evolving area of research. The relevance of it rests in its capacity to contribute to both oral and systemic disorders. The microbiome is present in biofilms throughout the oral cavity, creating an environment that promotes health by maintaining a delicate equilibrium. However, disruptions to this equilibrium can allow pathogens to proliferate and cause disease, resulting in a condition known as dysbiosis. The initial phase of human microbiome

Pathogenic Bacteria Associated with Periodontitis

research involves identifying the microbiome in a healthy state, followed by a deeper exploration of how it influences the functional and metabolic pathways associated with various diseased states.

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