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Review Article

Understanding Microbial Dysbiosis as a Key Driver in Oral Squamous Cell Carcinoma Pathophysiology

Vikram S Amberkar[1], Kochli Channappa Niranjan[2]

1-Professor, Department of Oral Pathology, College of Dental Sciences, Davangere, 2-Professor & Head, Department of Oral and Maxillofacial Pathology, SDM College of Dental Sciences and Hospital, Shri Dharmasthala Manjunatheshwara University, Dharwad

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Abstract

Oral squamous cell carcinoma (OSCC) presents a significant global health challenge, with established risk factors including tobacco use, alcohol consumption, and human papillomavirus (HPV) infection. Recent research has illuminated the role of the oral microbiome in OSCC pathogenesis, highlighting microbial dysbiosis—a disruption in microbial balance—as a potential contributor to disease development. This review examines how dysbiosis influences OSCC through altered microbial composition, chronic inflammation, production of carcinogenic metabolites, and biofilm formation. Pathogenic bacteria like Fusobacterium nucleatum and Porphyromonas gingivalis are implicated in fostering a pro-inflammatory milieu conducive to carcinogenesis. Additionally, microbial metabolites and biofilms play crucial roles in OSCC progression. The review underscores the promise of biomarkers and interventions such as probiotics, prebiotics, and targeted antimicrobial therapies in early detection and therapeutic strategies for OSCC. Future research directions should focus on optimizing these approaches to improve clinical outcomes while minimizing unintended consequences associated with oral microbiome modulation.

Keywords: Oral squamous cell carcinoma, oral microbiome, microbial dysbiosis, chronic inflammation, biofilm, Fusobacterium nucleatum, Porphyromonas gingivalis

Address for Correspondence:
Dr. Vikram S Amberkar, M.D.S
Professor, Department of Oral Pathology
College of Dental Sciences, Davangere-577004
Gmail: drvickys@gmail.com

INTRODUCTION

Oral squamous cell carcinoma (OSCC) is the most prevalent type of oral cancer, significantly impacting global health due to its high morbidity and mortality rates. Traditionally, risk factors such as tobacco use, alcohol consumption, and human papillomavirus (HPV) infection have been closely associated with the development of OSCC [1]. However, recent advancements in microbial research have brought to light the potential role of the oral microbiome in the pathogenesis of this disease. The human oral cavity hosts a complex and diverse microbial community, which, when imbalanced—a state known as dysbiosis—may contribute to various pathological conditions, including cancer.

Emerging evidence suggests that microbial dysbiosis in the oral cavity can influence OSCC through multiple mechanisms [2]. Changes in microbial composition, chronic inflammation, production of carcinogenic metabolites, and biofilm formation are some of the ways dysbiosis may promote cancer development. Pathogenic bacteria such as Fusobacterium nucleatum and Porphyromonas gingivalis have been particularly implicated in these processes. Understanding the intricate relationship between microbial dysbiosis and OSCC could pave the way for new diagnostic and therapeutic strategies, potentially improving early detection and patient outcomes in this challenging disease [3].

Impact of Microbial Composition Changes on OSCC Development:

Recent studies have revealed significant differences in the microbial diversity and composition in the oral cavities of OSCC patients compared to healthy individuals. In OSCC patients, there is a notable increase in pathogenic bacteria such as Fusobacterium nucleatum. This bacterium is known for its role in creating a pro-inflammatory environment, which can contribute to the initiation and progression of cancer [3]. The presence of Fusobacterium nucleatum in higher quantities may promote carcinogenesis through mechanisms such as invasion of epithelial cells, immune evasion, and enhancement of inflammatory responses, all of which create a conducive environment for cancer development.

Conversely, there is a marked decrease in beneficial bacteria, such as Streptococcus species, in OSCC patients. Streptococcus species play a crucial role in maintaining oral health by inhibiting the growth of pathogenic bacteria and contributing to the overall microbial balance. Their reduction disrupts this balance, allowing pathogenic bacteria to proliferate and dominate the oral microbiome [4]. This shift not only facilitates the survival and growth of harmful bacteria but also impairs the oral cavity's natural defenses against infection and inflammation, further exacerbating the risk of developing OSCC. The altered microbial composition thus highlights the critical role of microbial balance in oral health and disease, emphasizing the need for strategies to restore and maintain a healthy oral microbiome to potentially prevent or mitigate OSCC.

Mechanisms Linking Microbial Dysbiosis to Carcinogenesis in OSCC:

The mechanisms by which microbial dysbiosis contributes to carcinogenesis in oral squamous cell carcinoma (OSCC) are multifaceted, with chronic inflammation playing a pivotal role. Pathogenic bacteria, such as Porphyromonas gingivalis and Fusobacterium nucleatum, are known to induce robust inflammatory responses [5]. These bacteria can activate the host's immune system, leading to persistent inflammation and subsequent tissue damage. This chronic inflammatory state creates a microenvironment that supports cancer development by promoting cellular proliferation, inhibiting apoptosis, and facilitating genetic mutations [6][7].

In addition to inflammation, the production of carcinogenic metabolites by certain oral bacteria further exacerbates carcinogenesis. For instance, some bacteria generate acetaldehyde, a metabolite known for its DNA-damaging properties, which can lead to mutations and genomic instability. Moreover, immune evasion by specific pathogenic bacteria allows them to persist within the host, resulting in continuous infection and inflammation [7]. This persistent state undermines the host's immune surveillance, thereby increasing the risk of cancer. Together, these mechanisms underscore the complex interplay between microbial dysbiosis and OSCC, highlighting the critical need for strategies aimed at modulating the oral microbiome to prevent or mitigate cancer development.

Microbial Metabolites and Toxins:

Microbial metabolites and toxins produced by oral bacteria play a significant role in the carcinogenesis of oral squamous cell carcinoma (OSCC). One notable example is Fusobacterium nucleatum, which produces FadA adhesin. This adhesin can activate beta-catenin signaling, a pathway crucial for cellular proliferation and differentiation. When beta-catenin signaling is dysregulated, it can lead to uncontrolled cell growth, a hallmark of cancer. The activation of this pathway by FadA adhesin promotes the proliferation of cancer cells, contributing to tumor growth and progression . Additionally, other bacterial species in the oral cavity produce carcinogenic metabolites, such as acetaldehyde, which is derived from the metabolism of alcohol by bacteria like Streptococcus species. Acetaldehyde can cause DNA damage, leading to mutations and genomic instability, further promoting carcinogenesis in the oral epithelium [8].

The interaction between these microbial metabolites and host tissues underscores the complex role of the oral microbiome in cancer development. Metabolites like hydrogen sulfide and nitric oxide, produced by anaerobic bacteria, can induce oxidative stress and inflammation, creating a microenvironment that is conducive to cancer [8]. These metabolites not only directly damage DNA but also modulate the immune response, making it less effective in combating cancerous changes. Therefore, the production of microbial metabolites and toxins is a critical factor in the pathogenesis of OSCC, emphasizing the need for therapeutic strategies that target these microbial products to prevent or mitigate cancer development .

Biofilms: Stealthy Architects of Oral Cancer:

Biofilm formation is another crucial factor in the pathogenesis of oral squamous cell carcinoma (OSCC). Biofilms are structured communities of bacteria that adhere to surfaces and are embedded in a self-produced extracellular matrix. This matrix protects the bacteria from the host immune system and antibiotic treatments, allowing pathogenic bacteria to persist and thrive in the oral cavity. In the context of OSCC, biofilms can facilitate a chronic inflammatory state by continuously stimulating the host immune response. This persistent inflammation can lead to tissue damage and create a microenvironment that supports cancer development and progression. For instance, biofilms formed by Porphyromonas gingivalis and Fusobacterium nucleatum (Figure 1) are often associated with periodontal disease, which has been linked to an increased risk of OSCC [9] .

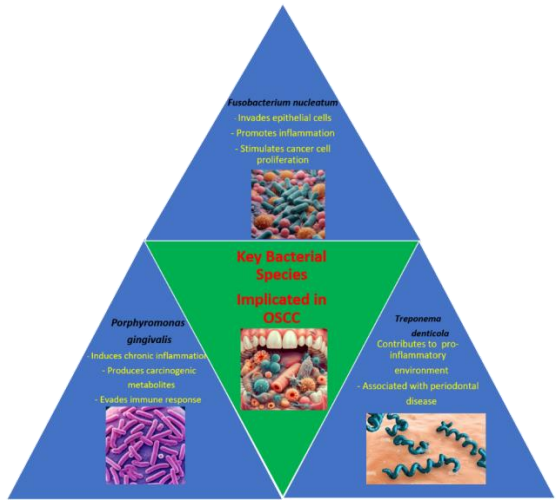

Figure 1: Key bacterial species implicated in OSCC

The protective nature of biofilms also enables the survival and proliferation of pathogenic bacteria in the oral cavity. This not only allows for the sustained production of carcinogenic metabolites and toxins but also enhances the ability of these bacteria to evade the host immune response. As a result, biofilms contribute to a cycle of persistent infection and inflammation, further promoting carcinogenesis. The presence of biofilms in OSCC patients highlights the importance of targeting these microbial communities in therapeutic strategies. Disrupting biofilm formation or enhancing biofilm penetration by antimicrobial agents could be crucial steps in reducing the microbial burden and associated inflammatory responses, potentially lowering the risk of OSCC progression [10].

Biomarkers for Early Detection:

The identification of altered microbial profiles in patients with oral squamous cell carcinoma (OSCC) suggests promising opportunities for biomarker development in early detection and diagnosis. Specific bacterial species or microbial signatures found in OSCC patients' oral microbiomes could serve as reliable biomarkers. Non-invasive techniques, such as saliva testing, could be refined and utilized for routine screening purposes, offering a potential breakthrough in identifying high-risk individuals at early stages of OSCC development. These biomarkers hold the potential to enhance current diagnostic strategies, enabling earlier intervention and improved clinical outcomes for patients [11].

Therapeutic Potential of Probiotics and Prebiotics:

Modulating the oral microbiome through probiotics and prebiotics presents a promising therapeutic avenue in managing OSCC. By introducing beneficial bacteria or promoting their growth, these interventions aim to restore microbial balance disrupted by pathogenic bacteria implicated in cancer progression [12]. Probiotics can potentially inhibit the growth of harmful microbes and enhance mucosal barrier function, while prebiotics provide nourishment for beneficial bacteria. Such approaches not only hold promise for reducing cancer risk but also for improving oral health outcomes overall. However, further research is needed to elucidate the specific strains and formulations that are most effective in mitigating OSCC risk and supporting oral microbiome health [13].

Targeted Antimicrobial Therapies for OSCC:

Targeted antimicrobial therapies aimed at specific pathogenic bacteria associated with OSCC could represent a novel approach in both prevention and treatment strategies. By selectively eradicating or suppressing harmful microbes, antimicrobial treatments aim to mitigate chronic inflammation and disrupt carcinogenic processes within the oral cavity. However, the challenge lies in preserving the delicate balance of the oral microbiome, which includes beneficial bacteria essential for maintaining oral health. Careful consideration and precise targeting of antimicrobial agents are crucial to avoid unintended consequences, such as promoting antibiotic resistance or exacerbating dysbiosis. Future research efforts should focus on developing tailored antimicrobial approaches that effectively target pathogenic bacteria while preserving overall oral microbiome integrity [14].

Conclusion:

In summary, the role of the oral microbiome in oral squamous cell carcinoma (OSCC) is complex and pivotal. Microbial dysbiosis, characterized by altered microbial composition, chronic inflammation, production of carcinogenic metabolites, and biofilm formation, creates an environment conducive to OSCC development. Pathogenic bacteria like Fusobacterium nucleatum and Porphyromonas gingivalis contribute significantly to carcinogenesis through their pro-inflammatory effects and immune evasion mechanisms. Additionally, microbial metabolites and biofilms further enhance cancer progression by inducing DNA damage and sustaining inflammatory responses. The identification of microbial biomarkers offers potential for early OSCC detection, while therapeutic strategies targeting the oral microbiome, such as probiotics, prebiotics, and targeted antimicrobial therapies, present promising avenues for disease management. Continued research is essential to refine these approaches, optimizing their clinical application and advancing personalized treatments for OSCC.

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Conflicts of interest
There are no conflicts of interest

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