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Oral microbiota and cancer – what is the current state of knowledge?

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Abstract

Background

Cancer is now second, right after cardiovascular diseases (CVD), cause of death in the world. Estimated death count by cancer in European Union in 2025 was 1 280 000. This number, complexity and diversity of cancers pose a challenge to identify more possible causes of the disease to improve treatment, prevention and early detection. One of documented factors, that can play a key role in cancer development are bacteria. Oral microbiota is one of the most complex in the human body. It has been shown that it plays an important role in various disease progression and formation. Hundreds of bacterial, species have been shown to be present in the human oral cavity.

Aim

The aim of this review is to summarize the current knowledge state of link between oral microbiome and cancer in terms of pathophysiology, risk factors, diagnostic features.

Material and methods

This study was designed as a literature review with elements of structured systematic approach. Studies were included if they were peer-reviewed original articles, meta-analysis, systematic reviews, or epidemiological studies focusing on oral microbiome effect on cancer. Case reports, expert opinions without original data, non-English publications, and abstracts without full-text availability were excluded from the analysis

Results

Results show that oral microbiota dysbiosis is present in many cancer types like oral cavity, digestive tract cancers, haematological cancers.

Conclusions

Oral microbiome alterations are widely present in many cases of different types of cancer. Further studies are vital to determine whether or not, there should be more screening, prevention and treatment of oral dysbiosis as cancer preventive measures.

Keywords: cancer, microbiome, dysbiosis, oral microbiome,

Introduction

Cancer is now second, right after cardiovascular diseases (CVD), cause of death in the world. Estimated death count by cancer in European Union in 2025 was 1 280 000. [1] This number, complexity and diversity of cancers pose a challenge to identify more possible causes of the disease to improve treatment, prevention and early detection. [2] One of documented factors, that can play a key role in cancer development are bacteria. The best, and well known type I carcinogenic bacteria is *Helicobacter pylori* which plays a role in gastric cancer development. [4] However, many other bacteria species, and microbiota shifts were documented as risk factors for cancer development.

Oral microbiota is one of the most complex in the human body. It has been shown that it plays an important role in various disease progression and formation. [3] Hundreds of bacterial species have been shown to be present in the human oral cavity. [5] This is due to many surfaces and types of tissues present. We can divide them to hard tissues: teeth and soft, mucosal tissues: tongue, buccal mucosa, gingiva, palate. [6] Each of them plays a role in diversity of microbiome. There are also many factors that play a role in oral microbiota composition like oral hygiene, alcohol, tobacco, age, dietary habits, genetics, pregnancy, medications and social status. [7]

Oral microbiota mainly is formed by Actinobacteria, Bacteroidetes, Chlamydia, Euryarchaeota, Fusobacteria, Firmicutes, Proteobacteria, Spirochaetes, Tenericutes. [8] Fungi account for 0.004% of all microorganisms in oral cavity. [9] Physiologically, normal oral microbiome plays

a role in oral and general health. It balances pH, suppress pathogen growth, some authors indicate a role in CVD homeostasis. [10] However, oral microbiota shift to dysbiotic state may play a part in pathophysiology of many diseases including arthritis, colorectal and pancreatic cancers, inflammatory bowel diseases.[10,11] This pathological state of microbiome leads to chronic inflammation. Chronic inflammation is key feature and documented factor in development of various diseases including cancer. [12,13]

The aim of this review is to summarize the current knowledge state of link between oral microbiome and different types of cancer.

Materials and methods

This study was designed as a literature review with elements of structured systematic approach. The aim was to evaluate the current evidence of oral microbiome impact on cancer in human. A search of the literature was performed using the following electronic databases: PubMed Scopus, Web of Science and Google Scholar. In addition, manual screening of reference lists from relevant articles was conducted to identify further eligible publications.

The search strategy was based on combinations of keywords including: “oral microbiome cancer”, "oral cancer microbiome", “dysbiosis of oral microbiota and cancer”, “microbiome and cancer”. The search included articles published between 2000-2026 with preference toward the most recent publications.

Studies were included if they were peer-reviewed original articles, meta-analysis, systematic reviews, or epidemiological studies focusing on oral microbiome effect on cancer. Case reports, expert opinions without original data, non-English publications, and abstracts without full-text availability were excluded from the analysis.

Results

Dysbiosis as a risk factor of cancer development

Cancers of lip, oral cavity and pharynx (LOCP) were diagnosed in 758000 people worldwide in 2022 posing a significant public challenge. Oral cancer represents 42% of cases in this group. The most common oral cancer is squamous cell carcinoma (SSC) which originates from oral mucosa. [14] Prognoses indicate increased burden of oral cancer in the future. [15] Amongst

most common factors like use of tobacco, *Human Papillomavirus* (HPV), bad hygiene, chronic mechanical irritation of mucosal tissues, oral microbiome also plays its role in cancer development in oral cavity. Importantly, 15% of oral cancers can't be attributed to aforementioned factors posing a challenge in exploration of other risk factors. [16]

Shifts in oral microbiota populations towards, for example *Porphyromonas gingivalis*, which are obligatory anaerobic and their fermentation products are associated with chronic inflammation. Chronic, uncontrolled inflammation may promote malignant cell transformation in the focal tissue. [17] If remained uncontrolled, it can later result in tumor progression, angiogenesis and distant metastases. Hypoxic environment of malignant tumors may promote this process even further. [18]

In study conducted by Zhao et al., bacterial dysbiosis was observed within SCC surface lesion samples (80 individual samples were collected from patients with SCC) with drastic changes in bacterial composition and bacterial gene functions in comparison to controls. However, the authors declared that it was difficult to determine whether the bacterial dysbiosis were playing a role in carcinogenesis of SCC or the SCC drove the change in bacterial function. [19]

Periodontal disease (PD) is one of the most common oral conditions, which is characterised by chronic inflammation and destruction of tissues supporting the tooth caused by Gram-negative anaerobic bacteria in the dental biofilm. [20] PD results in a chronic release of bacterial and inflammatory particles into the saliva and bloodstream. [21] The most important cause of periodontitis are aforementioned bacteria *Porphyromonas gingivalis* which can alter the physiological biofilm and create environment favourable for induction of periodontitis. [22] Some authors show evidence that PD is significantly associated with an increased risk of hematopoietic and lymphatic cancers, especially lymphatic cancers. It is also worth noting that this association is especially strong in non-smokers populations, which suggests even bigger influence of disrupted microbiome in oral cavity which may be the result of bad oral health and hygiene. [23] Meta-analysis conducted by Yao et al. showed that PD is significantly associated with an increased risk of oral cancer [OR = 3.53, 95%CI (1.52 – 8.23); p=0.003]. [24] Basing on this research it is important to highlight the importance of proper oral hygiene to prevent PD. However, some authors report that using mouthwash, both alcoholic and non-alcoholic was significantly associated with oral and pharyngeal non-squamous cell carcinoma (NSCC). Non-alcoholic mouthwash was associated with bigger risk than alcoholic one. [25] The same author also found that PD is a significant risk factor for NSCC. Freudenheim et al. conducted a prospective cohort study in which they measured occurrence of postmenopausal breast cancer

in patients. PD was reported in 26.1% of patients. The PD was accounted for an increased risk of cancer with hazard ratio (HR) of 1.14. [26]

In many studies *P. gingivalis* was associated with an increased risk of pancreatic cancer (PC). Michaud et al. in their prospective study, compared antibodies against *P. gingivalis* in PC patients (PC diagnosis was subsequent to antibodies testing). Patients with antibodies level >200ng/mL had almost 2-fold higher risk of developing PC. Interestingly, patients with high levels of antibodies to common commensal oral bacteria had almost 50% smaller risk of developing PC. [27]

To summarize dysbiosis possible effect on cancer development, we summarize it into tables.

Table 1. Oral microbiome dysbiosis and head and neck cancer (HNC) risk

Type of cancer	Bacteria (increased)
Oral cancer (NSCC, SSC)	<i>P. gingivalis</i> <i>Actinobacteria</i> <i>Moraxella</i> <i>Veillonella</i> <i>Bacillus</i> <i>Periodonticum</i> <i>Bacteroidetes</i> <i>Fusobacterium nucleatum</i> <i>Prevotella intermedia</i> <i>Prevotella tannerae</i> <i>Aggregatibacter segnis</i> <i>Peptostreptococcus stomatis</i>
Tongue/pharynx cancer	<i>P. gingivalis</i> <i>Neisseria</i> <i>Fusobacterium nucleatum</i> <i>Streptococcus parasanguinis</i> <i>Streptococcus sanguinis</i> <i>Corynebacterium</i>
Gingival SCC	<i>P. gingivalis</i> <i>Fusobacterium</i> <i>Peptostreptococcus</i>

	<i>Prevotella</i> <i>Streptococcus</i> <i>Neisseria</i> <i>Haemophilus</i>
Nasopharyngeal carcinoma	High biodiversity of microbiome

Regarding HNC, the most prevalent bacteria were *P. gingivalis*, *Fusobacterium*, *Neisseria*. As previously mentioned, *P. gingivalis* is responsible for increased risk of many cancers. This table presents which bacteria species are increased in particular cancers of head and neck, highlighting their possible role in malignancy progression and formation. [28–53] Data provides information about possible carcinogenic mechanisms of Firmicutes and Bacteroides. Due to their fermentation of host's excessive protein into nitrosamines and sulfides which may promote malignant transformation of host cells because of their capabilities to damage deoxyribonucleic acid (DNA). [54,55]

Table 2. Oral microbiome dysbiosis and gastrointestinal cancer (GIC) risk.

Type of cancer	Bacteria (increased)	Bacteria (decreased)
Esophageal cancer (EC): Squamous cell and adenocarcinoma	<i>Streptococcus anginosus</i> <i>Streptococcus mitis</i> <i>Treponema denticola</i> <i>Negativicutes</i> <i>Firmicutes</i> <i>Prevotellaceae</i> <i>Prevotella</i> <i>Selenomonadales</i> <i>Veillonellaceae</i> <i>P. gingivalis</i> <i>Corynebacterium</i>	<i>Proteobacteria</i> <i>Neisseriaceae</i> <i>Neisseriales</i> <i>Betaproteobacteria</i> <i>Gammaproteobacteria</i> <i>Neisseria</i> <i>Streptococcus pneumoniae</i> <i>Lautropia</i> <i>Bulleidia</i> <i>Catonella</i> <i>Peptococcus</i> <i>Cardiobacterium</i> <i>Moryella</i>
Pancreatic cancer (PC)	<i>P. gingivalis</i> <i>Periodonticum</i>	<i>Proteobacteria</i> <i>Fusobacteria</i>

	<i>Streptococcus</i> <i>Leptotrichina</i> <i>Aggregatibacter</i> <i>Granulicatella adiacens</i> <i>Enterobacteriaceae</i> <i>Lachnospiraceae</i> G7 <i>Staphylococcaceae</i> <i>Bacteroidaceae</i> <i>Firmicutes</i> <i>Fusobacterium nucleatum</i>	<i>Leptotrichia</i> <i>Neisseria</i> <i>Streptococcus mitis</i> <i>Neisseria elongata</i> <i>Porphyromonas</i> <i>Haemophilus</i> <i>Paraprevotella</i>
Colorectal cancer (CRC)	<i>P. gingivalis</i> <i>Fusobacterium</i> <i>Lactococcus</i> <i>Prevotella</i> <i>Veillonella</i> <i>Lactobacillus</i>	<i>Rothia</i> <i>Clostridia</i> <i>Pseudomonas</i>
Gastric cancer (GC)	<i>P. gingivalis</i> <i>Prevotella</i> <i>Veillonella</i> <i>Actinomyces</i> <i>Aggregatibacter</i> <i>Corynebacterium</i> <i>Streptococcus</i> <i>Firmicutes</i> <i>Streptococcus</i>	<i>Haemophilus</i> <i>Neisseria</i> <i>Porphyromonas</i> <i>Peptostreptococcus</i> <i>Fusobacterium</i>
Liver cancer (LC)	<i>Oribacterium</i> <i>Fusobacterium</i> (more studies are required)	

This table highlights what type of microbiome dysbiosis is mainly present in patients with GIC. [56–85]

As in HNC, *P. gingivalis* is found to be the most common bacteria which level is increased in GIC patients. *P. gingivalis* is followed by *Prevotella*, *Veillonella*. This creates a room to further study and discover their role in pathogenesis of gastrointestinal cancers.

As for liver cancer, very small number of studies are published regarding oral microbiome dysbiosis and its potential effect on carcinogenesis. However, detection of *Oribacterium* and *Fusobacterium* are believed to be useful as a diagnostic tool to discriminate healthy patients from liver cancer patients. [86]

Discussion

This article aimed to summarize link between oral microbiome dysbiosis and cancer. As highlighted, many bacteria species levels are disrupted even before the malignancy is diagnosed. This creates an opportunity for further research in terms of diagnostic features in the future.

As shown in tables, there is a vast variety of microbiome disruption in different forms of cancer. This poses a significant challenge for researchers to develop appropriate and precise diagnostic and therapeutic tools. Despite that, nowadays we are given solid evidence that microbiome dysfunction may lead to cancer. Not only oral cancer but many different types of cancer. As mentioned, cancer is now 2nd leading cause of death in the world. This puts additional pressure to understand better the exact role of microbiome dysbiosis in pathophysiology role in malignancies.

This article also highlights some of the conditions where the microbiome dysbiosis is present and predisposes to malignant transformation of healthy host cells. Chronic inflammation is one of the key factors which may lead to cancerous transformation of cells. [87] Due to genetic factors, poor oral hygiene, alcohol or tobacco use microbiome can shift toward pathogenic bacteria which may cause aforementioned condition. [88–90].

Furthermore, oral microbiota dysbiosis can be diagnostic factor for cancer. For instance, the study from Zhang et al. suggests that certain oral based microbiota biomarkers can be used as an additional tool for colorectal cancer risk prediction.[91] Su et al. demonstrated that oral microbiota dysbiosis can be a diagnostic marker for OSSC. They discovered that certain strains of *Fusobacterium nucleatum* are elevated, whilst other bacteria and tumor-suppressing metabolites are at lower level. [92] However, to further develop appropriate approaches when it

comes to diagnostic features, identification of highly specific oral microbiomes is necessary.
[93]

Conclusion

As seen, oral microbiome alterations are widely present in many cases of different malignancies. The exact role of bacteria in neoplasms formation is yet to be discovered, however there are suspected mechanisms like chronic inflammation, synthesis of carcinogenic compounds which promotes mutations in healthy host cells. Further studies are vital to determine whether or not, there should be more screening, prevention and treatment of oral dysbiosis as cancer preventive measures.

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