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THE ROLE OF ORAL CAVITY HEALTH IN PATHOGENESIS OF GASTROINTESTINAL MALIGNANCIES

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Abstract: Gastric cancer remains a significant global health concern, necessitating multifaceted preventive strategies. Recent research highlights the intricate interplay between oral health and gastric cancer risk, suggesting that maintaining optimal oral cavity health may contribute to reducing the incidence of this malignancy. This review paper summarizes current evidence on the association between oral health and gastric cancer and provides practical recommendations for clinicians and public health practitioners to integrate oral health strategies into gastric cancer prevention efforts. It is a systematic literature review focusing on clinical outcomes related to oral health in gastric cancer patients, utilizing databases such as PubMed and Web of Science, encompassed studies from 2000 to 2024 to comprehensively analyze the relationship between gastric cancer and oral health. It was identified that factors affecting the oral cavity health, as well as, contributing to the development of gastric cancer include inadequate oral hygiene with overgrowth of harmful bacteria, including Helicobacter pylori, periodontal disease and chronic inflammation, edentulism and associated gastroesophageal reflux disease, altered oral microbiota composition, alongside poor dietary habits. Given the intimate physiological and pathological connections between the oral cavity and the gastrointestinal tract, understanding and leveraging oral health strategies may offer novel avenues for gastric cancer prevention, ultimately leading to better patient outcomes and quality of life.

Introduction

Historically, oral health was often viewed in isolation from the rest of the body. This perspective has significantly shifted, with emerging research highlighting the profound impact of oral conditions on systemic health. The oral cavity acts as a gateway to the body, where signs of systemic diseases often manifest first or where poor oral health can cause or exacerbate medical conditions. One of the prime examples of this interconnection is the relation of gastrointestinal malignancies, especially gastric cancer, with inadequate oral cavity health.

Gastric cancer ranks as the fifth most prevalent cancer and the fourth leading cause of cancer-related mortality globally, posing a significant public health concern worldwide. [17] Although the pathogenesis of gastric malignancies is multifactorial, increasing evidence suggests a correlation between the composition of oral microbiota and the carcinogenesis of gastric tumors. The oral microbiota represents a complex ecosystem within the human body, housing over 700 bacterial species, including such bacteria as Helicobacter pylori. This literature review aims to investigate the critical connection between oral cavity health and gastrointestinal malignancies, emphasizing the significance of this relationship in dental practice.

Methods

The methods section outlines the comprehensive approach taken to explore the impact of gastric cancer on oral health. A systematic literature review was conducted, utilizing databases such as PubMed, Web of Science, Springer Nature, BMC microbiology, MDPI, JCO. Keywords included "gastric cancer," "oral health," "dental effects," and "systemic disease impact." Inclusion criteria were studies published in English, from 2000 to 2024, focusing on clinical outcomes related to oral health in gastric cancer patients. Exclusion criteria encompassed studies on pediatric populations

and those lacking clear oral health outcomes. The selection process involved initial screening based on titles and abstracts, followed by full-text reviews to determine final inclusion. Quality assessment of the studies was performed using standardized checklists. Data extraction focused on study design, participant demographics, types of oral health impacts observed, and the statistical significance of findings. This rigorous methodology ensures a comprehensive synthesis of existing literature, providing a solid foundation for understanding the intricate relationship between gastric cancer and oral health.

Results

Oral microbiota and Helicobacter pylori (H. pylori) transmission: Inadequate oral hygiene can lead to an overgrowth of harmful bacteria in the oral cavity, including H. pylori. H. pylori is a bacterium associated with gastric cancer, as it can colonize the stomach lining and contribute to the development of gastric inflammation, ulcers, and eventually cancer. Poor oral hygiene increases the likelihood of H. pylori colonization in the oral cavity, which can then be swallowed and contribute to gastric cancer development.

Oral infections and chronic inflammation: Neglecting oral health can lead to conditions such as periodontal disease and dental caries, which are characterized by chronic inflammation and bacterial infections. Chronic inflammation in the oral cavity can promote systemic inflammation, which is associated with an increased risk of various cancers, including gastric cancer. The inflammatory mediators produced in response to oral infections may contribute to the initiation and progression of gastric cancer.

Gastroesophageal reflux disease (GERD): Poor oral health, such as dental erosion and tooth loss, can impair chewing and swallowing abilities, leading to an increased risk of GERD. GERD is characterized by the reflux of stomach acid into the esophagus, which can cause chronic irritation and inflammation of the esophageal mucosa. Persistent GERD can lead to Barrett's esophagus, a precancerous condition, and increase the risk of developing esophageal cancer.

Altered oral microbiota composition: Poor oral hygiene practices can alter the composition of the oral microbiota, leading to dysbiosis and overgrowth of harmful bacteria. Dysbiosis in the oral microbiota has been associated with various systemic conditions, including gastric cancer. Changes in the oral microbiota composition may contribute to systemic inflammation and immune dysregulation, which can promote carcinogenesis in the stomach.

Poor nutrition and dietary habits: Individuals with poor oral health may experience difficulties in chewing and swallowing, leading to dietary restrictions and preferences for soft, processed foods that are high in sugar and low in fiber. A diet high in processed foods and low in fruits and vegetables is associated with an increased risk of gastric cancer. Additionally, poor oral health can impair nutrient absorption and lead to malnutrition, which can weaken the immune system and increase susceptibility to cancer.

Discussion

Poor oral cavity health can potentially contribute to the development of gastric cancer through several mechanisms outlined in the paragraphs below.

Oral microbiota and H. pylori transmission

The oral cavity harbors one of the most intricate and densely populated bacterial communities known, encompassing over 700 bacterial species identified through ribosomal RNA (rRNA) gene-based techniques [1,11]. Microbial communities, increasingly recognized as pivotal in gastric cancer incidence and progression, exhibit enrichment of various bacterial genera and species, many

of which commonly inhabit the oral cavity. Noteworthy is the presence of species such as Helicobacter pylori, Fusobacterium, Aggregatibacter, Streptococcus, Lactobacillus, and Lactococcus in gastric patients (see Figure 1).

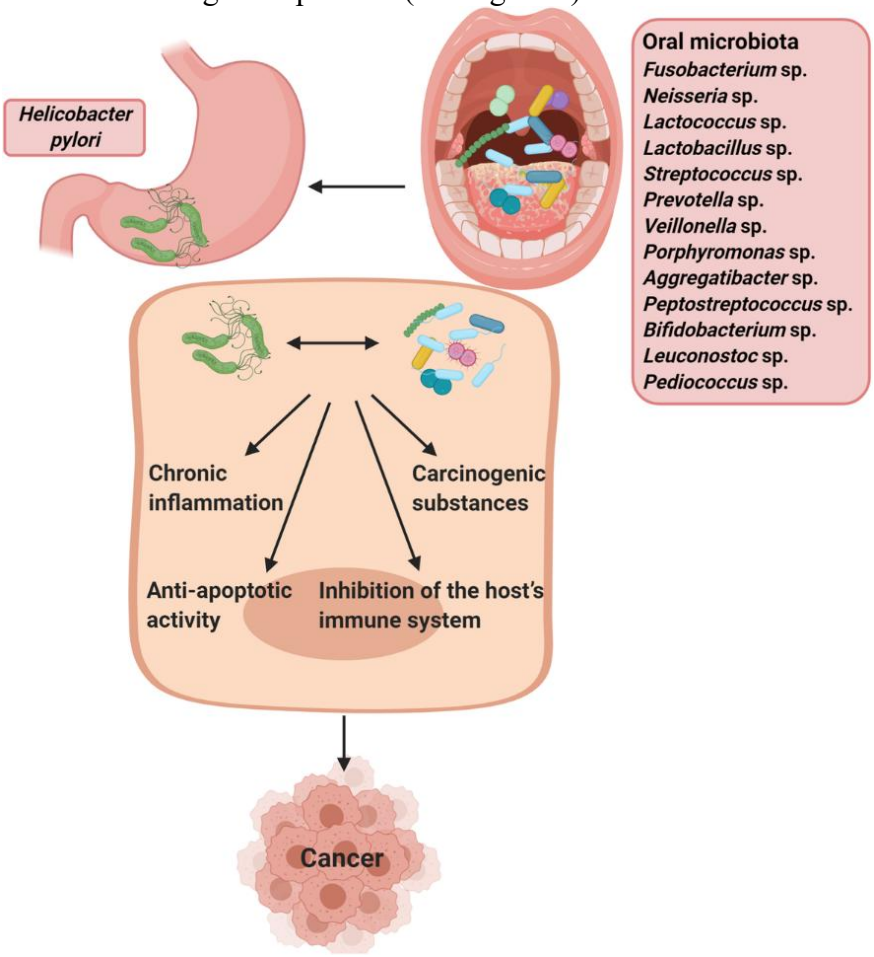


Figure 1. Potential mechanisms of oral microbiota include the induction of chronic inflammation, the inhibition of the host's immune system, the anti-apoptotic activity, and the carcinogenic substances that may promote cancer.

Notably, poor oral hygiene can lead to the accumulation of bacterial plaque on teeth and gums, creating an environment conducive to the growth of pathogenic bacteria, including Helicobacter pylori. H. pylori is typically associated with gastric ulcers and gastric cancer. While the exact route of transmission is not fully understood, evidence suggests that oral-oral and fecal-oral routes may play a role. Studies have shown that H. pylori can survive in the oral cavity, particularly in dental plaque, saliva, and on the surface of the tongue. From there, it can be ingested and reach the stomach, where it colonizes the gastric mucosa. Once in the stomach, H. pylori can induce chronic inflammation, which is a key factor in gastric carcinogenesis. Moreover, H. pylori disturbs microbial balance through alterations in nutrient availability, gastric acidity, and immune response, facilitating the overgrowth and colonization of non-H. pylori bacteria. It also produces toxins and enzymes that damage the gastric epithelium and promotes the development of gastric ulcers and cancer [2,12,16].

Oral infections and chronic inflammation

Periodontal disease, characterized by inflammation and infection of the gums and supporting structures of the teeth, is one of the most common oral infections associated with poor oral hygiene. Periodontal disease is a silent, chronic, painless and communicable bacterial infection that often goes undetected or ignored until stages of moderate and advanced periodontitis, when severe gum and bone destruction is unbearable and no longer able to be ignored. Left untreated gum disease can cause tooth loss (see Figure 2) [3,13]. Pathogenic bacteria from oral plaque serve as primary agents in periodontitis etiology, whereas various local factors such as calculus, smoking, and iatrogenic elements contribute to its development. Systemic factors including endocrine disorders, immune deficiencies, medications, stress, and age are implicated as risk indicators. Socransky et al. categorized subgingival biofilm into five microbial complexes, with one particularly enriched in aggressive bacteria like Fusobacterium nucleatum, which play a crucial role in periodontal pathogenesis. Fusobacterium nucleatum, a Gram-negative anaerobic bacterium, contributes to the development and progression of periodontitis through its ability to form biofilms, induce inflammation, interact with other pathogens, and invade periodontal tissues. [15] Chronic inflammation in the oral cavity can lead to the production of inflammatory cytokines and reactive oxygen species, which can promote systemic inflammation and contribute to the development and progression of cancer. [18] Chronic inflammation may create a favorable microenvironment for cancer initiation and growth. Numerous studies have shown associations between periodontal disease and an increased risk of various cancers, including gastric cancer. For example, the study by Kwon et al. (2004). conducted in South Korea, discussed the potential link between chronic periodontitis and stomach cancer in the Korean population. In that study, data from over 10,000 people with gastric cancer and 40,000 healthy individuals in men under 65 years old were analyzed. The results revealed that individuals who had gum disease in the past one to two years were more likely to develop stomach cancer [4,14].

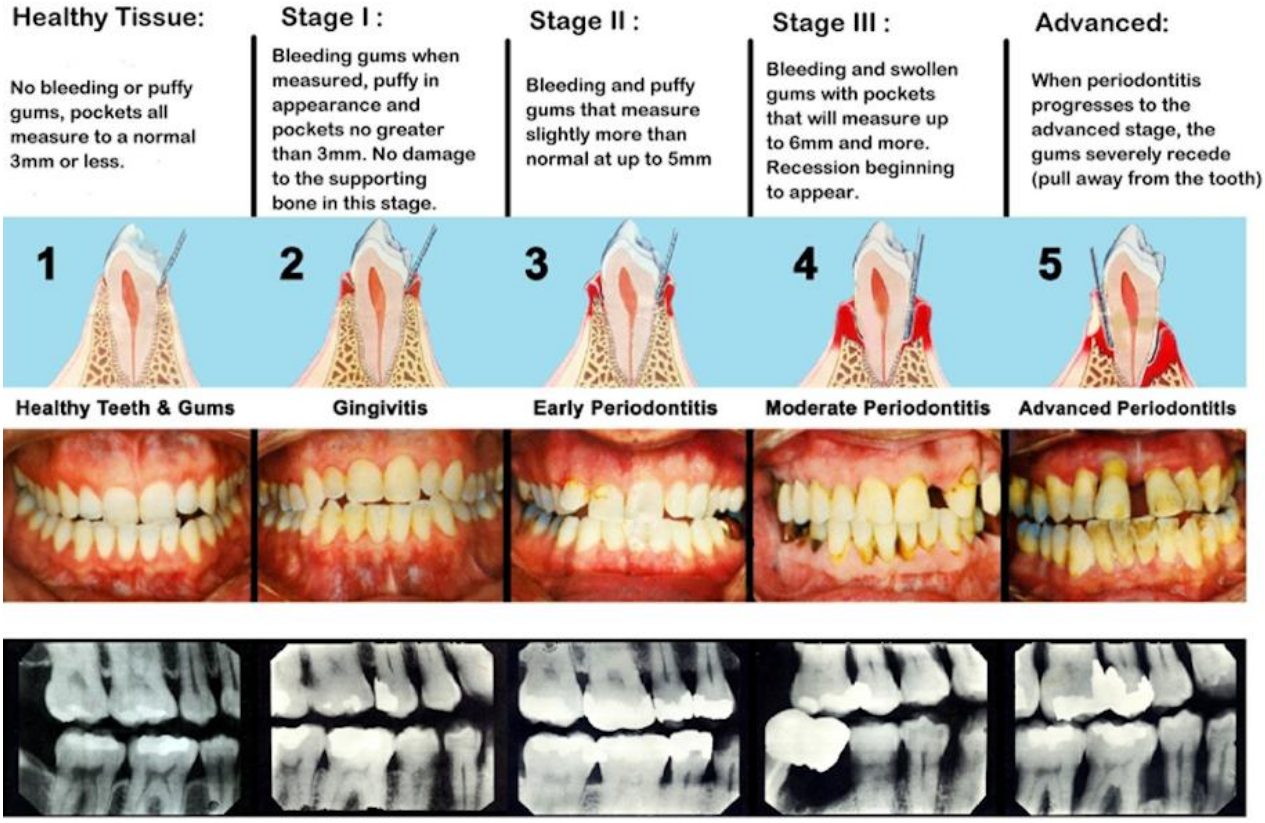


Figure 2. Stages of periodontal disease.

Edentulism and gastroesophageal reflux disease

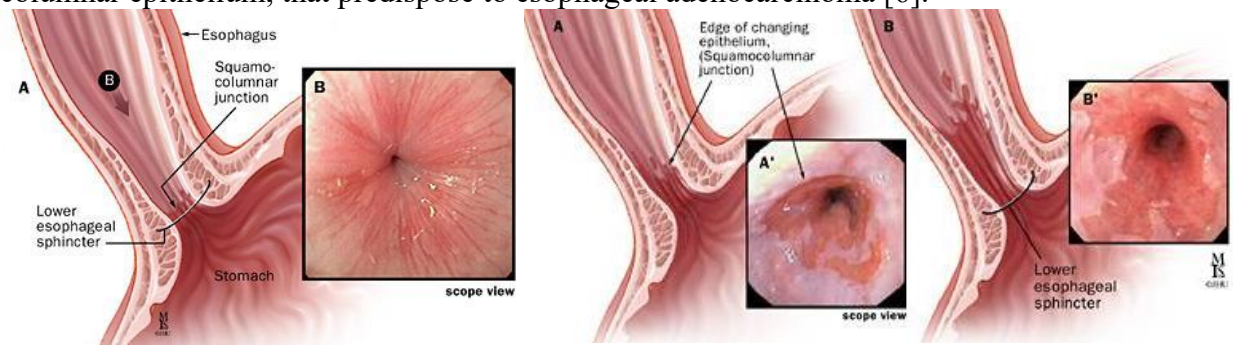
Proper chewing is essential for breaking down food into smaller particles, facilitating digestion and absorption in the stomach and intestines. Impaired chewing and swallowing, frequently stemming from poor oral health, can significantly contribute to the development or worsening of gastroesophageal reflux disease (GERD) through various mechanisms.

Firstly, inadequate chewing, often associated with dental issues such as tooth decay or missing teeth, leads to incomplete breakdown of food, resulting in larger food particles passing through the esophagus into the stomach, requiring more forceful contractions of the esophagus to propel them downward, thus increasing the likelihood of esophageal exposure to stomach acid and gastric contents, leading to irritation and inflammation of the esophageal lining characteristic of GERD. thereby increasing the likelihood of GERD symptoms such as acid reflux and heartburn [5].

Additionally, difficulties in swallowing can delay the transit of food from the mouth to the stomach, causing food to remain in the stomach for longer periods, elevating pressure within the stomach and promoting reflux of stomach contents into the esophagus. Furthermore, individuals with impaired chewing or swallowing may opt for softer, processed foods over fibrous fruits and vegetables or lean meats, which can exacerbate GERD by promoting weight gain, altering gut microbiota composition, and delaying gastric emptying.

Moreover, proper chewing stimulates saliva production, which helps neutralize stomach acid and protect the esophageal lining from damage caused by acid reflux. Reduced saliva production in individuals with impaired chewing or swallowing further increases the risk of GERD symptoms.

GERD is a chronic condition characterized by the reflux of stomach acid into the esophagus, leading to symptoms such as heartburn, regurgitation, and chest pain. Chronic exposure of the esophageal mucosa to gastric acid can lead to inflammation, erosions, and ulcerations. Over time, this can promote the development of Barrett's esophagus, a precancerous condition characterized by changes in the lining of the esophagus, namely metaplasia of squamous epithelial mucosa to columnar epithelium, that predispose to esophageal adenocarcinoma [6].



Figire 3. Development of Barret's esophagus.

Altered oral microbiota composition

The oral microbiota is a diverse community of bacteria that inhabit various oral surfaces, including the teeth, gums, tongue, and cheeks. [19] Poor oral hygiene practices, such as infrequent brushing and flossing, can disrupt the balance of the oral microbiota, leading to dysbiosis. Dysbiosis in the oral microbiota has been associated with various systemic conditions, including gastrointestinal diseases and cancer. Changes in the oral microbiota composition may promote inflammation, immune dysregulation, and metabolic alterations, all of which can contribute to carcinogenesis in the stomach and other organs [7,20].

Poor nutrition and dietary habits

Poor oral health, such as dental pain, tooth loss, and difficulty chewing, can affect dietary habits and food choices. Individuals with poor oral health may avoid hard, fibrous foods and prefer soft, processed foods that are high in sugar and low in fiber. This can lead to a diet that is deficient in essential nutrients, including vitamins, minerals, and antioxidants. A diet high in processed foods and low in fruits and vegetables is associated with an increased risk of gastric cancer. Conversely, a diet rich in fruits, vegetables, whole grains, and lean proteins is associated with a reduced risk of cancer. Poor oral health can also impair nutrient absorption and digestion, leading to malnutrition and weakened immune function, which can increase susceptibility to cancer and other diseases [8].

Specific manifestations of gastric cancer

Early detection of gastric cancer is paramount for effective management and improved patient outcomes. Recognizing the subtle yet significant signs and symptoms associated with the disease is crucial in facilitating timely diagnosis.

Common early manifestations of gastric cancer include dyspeptic symptoms such as epigastric discomfort, bloating, and early satiety. Gastrointestinal bleeding, either overt or occult, may present as hematemesis, melena, or occult blood in the stool. Progressive anorexia and unintentional weight loss are often observed, reflecting cancer cachexia. Persistent nausea and vomiting, particularly postprandial, may indicate gastric outlet obstruction.

In addition, constitutional symptoms such as fatigue, malaise, and generalized weakness may accompany early-stage gastric cancer, often attributed to anemia secondary to chronic gastrointestinal bleeding or tumor-related cytokine release.

Given the nonspecific nature of these symptoms, a high index of suspicion is warranted, particularly in individuals over 55 years of age or those with relevant risk factors. Prompt referral for endoscopic evaluation and biopsy confirmation is essential for timely diagnosis and initiation of appropriate management strategies, thereby optimizing patient outcomes in the context of gastric cancer [9].

Prevention

To effectively integrate oral health into gastric cancer prevention, a multi-faceted approach is essential. This includes promoting regular dental care to facilitate early detection and management of oral health conditions such as periodontal disease and dental caries. Emphasizing proper oral hygiene practices can minimize the accumulation of oral pathogens and reduce the risk of bacterial translocation, thus contributing to gastric cancer prevention. Comprehensive tobacco cessation programs and alcohol harm reduction strategies are crucial in addressing modifiable risk factors for both oral and gastric cancers.

Overall, addressing poor oral cavity care through regular dental check-ups, proper oral hygiene practices, a balanced diet, and management of risk factors such as GERD is crucial for reducing the risk of gastric cancer and other systemic conditions. Interdisciplinary collaboration between dental and medical professionals ensures comprehensive patient care and early detection of oral and gastrointestinal pathologies. Health education and promotion efforts can raise awareness about the link between oral health and gastric cancer risk, while research and policy advocacy support evidence-based interventions and policies to improve cancer prevention outcomes. By integrating these strategies into clinical practice, public health programs, and policy initiatives, we can advance efforts to reduce the global burden of gastric cancer and improve population health outcomes [10].

Conclusion

To conclude, gastric cancer presents a substantial global health challenge, necessitating comprehensive preventive measures. Recent studies demonstrate the intricate relationship between oral health and gastric cancer risk, proposing that maintaining optimal oral cavity health may help reduce cancer incidence. This systematic literature review summarizes current evidence on the correlation between oral health and gastric cancer, drawing from studies conducted between 2000 and 2024 and utilizing databases including PubMed and Web of Science. Factors contributing to both oral cavity health and gastric cancer development, such as inadequate oral hygiene, Helicobacter pylori infection, periodontal disease, chronic inflammation, edentulism and gastroesophageal reflux disease, altered oral microbiota composition, and poor dietary habits, have been identified. Understanding the close physiological and pathological connections between the oral cavity and the gastrointestinal tract highlights the potential of integrating oral health strategies into gastric cancer prevention efforts. This review emphasizes the evolving perspective of oral health's systemic impact, particularly evident in the interconnection between oral conditions and gastrointestinal malignancies like gastric cancer and esophageal cancer thus advocating for improved patient outcomes and quality of life through the implementation of effective oral health interventions.

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