Oral Cancer at a Glance

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Abstract

Overview: This review aims to serve as a comprehensive resource for healthcare professionals, researchers, and students interested in oral cancer, providing them with up-to-date information and insights into the current state of knowledge and practice in the field. Oral cancer, also known as mouth cancer, is a type of cancer that affects the mouth, tongue, lips, or throat. It is a common form of cancer worldwide, and its incidence is increasing annually. Oral cancer can be life-threatening if not detected early and treated promptly. Methods: We searched the PubMed database, Web of Science (WOS), Google Scholar, Scopus, and selected studies by predefined eligibility criteria. This review aims to provide an overview of oral cancer, including its causes, risk factors, signs and symptoms, diagnosis, treatment options, and prevention strategies. Result: Oral cancer is a preventable disease, and ongoing research is providing valuable insights into its risk factors and development. With this increasing knowledge, healthcare professionals have the opportunity to improve clinical outcomes by developing better early detection and treatment strategies. By staying up-to-date with the latest advancements in biomedical sciences and dentistry, they can make a significant impact on patient outcomes and save lives. Conclusion: summarizing the key points discussed in the review and highlighting the significance of continued research and awareness efforts to combat this complex and aggressive disease.

Keywords: Oral cancer- Diagnosis- Treatment- Prevention strategies- Risk factors- Symptoms

Introduction

Oral cancer, also referred to as mouth cancer, is a type of malignancy that impacts the oral cavity, including the lips, tongue, cheeks, gums, floor of the mouth, and throat [1]. This form of cancer can arise in various regions of the mouth, manifesting as a painless white lesion that gradually thickens, develops red spots, and eventually evolves into an ulcerative lesion. On the lips, it often appears as a chronic non-healing ulcer that steadily enlarges over time [2]. Additional indicators of oral cancer may consist of dysphagia, odynophagia, neck swelling, and sensations of numbness in the lips. Awareness of these symptoms is crucial for early detection and optimal treatment outcomes [3,4]. The World Health Organization (WHO) introduced a paradigm shift in 2005 by recommending a change in the classification of precancerous lesions to “potentially malignant disorders” (PMDs). This move was motivated by the observation that the majority of oral squamous cell carcinoma (OSCC) cases had evolved from preceding precancerous lesions. The PMDs encompass a spectrum of conditions, including leukoplakia, erythroplakia, oral lichen planus, oral submucosal fibrosis, actinic keratosis, discoid lupus erythematosus, and palatal lesions potentially induced by smoking. These disorders are characterized by their heightened propensity for malignant transformation relative to other oral pathologies [5]. Oral cancer has a poor
oral squamous cell carcinoma (OSCC) is a preventable disease that is primarily caused by environmental factors, with tobacco being the leading culprit. The development of OSCC is directly related to the dose, frequency, and mode of exposure to carcinogens, which are substances that have the potential to cause cancer. In addition to tobacco smoke, other known carcinogens that can contribute to the development of OSCC include excessive alcohol consumption, certain viruses such as human papillomavirus types 16 and 18, and prolonged exposure to ultraviolet (UV) light. By avoiding these carcinogens and adopting healthy lifestyle habits, individuals can significantly reduce their risk of developing this disease [2,17].

**Tobacco**

Tobacco usage is a primary contributor to the development of oral cancer, as it triggers genetic alterations in the buccal cells that can culminate in malignancy. The carcinogenic properties of tobacco are attributed to the chemical compounds present in cigarette smoke and other tobacco products, which instigate mutations in the cellular DNA, thereby increasing the likelihood of cancerous growth in the oral cavity [3,18-20].

**Alcohol**

Heavy alcohol consumption has been linked to an elevated risk of developing oral cancer. The reason for this association is that excessive alcohol consumption can cause damage to the cells in the mouth, making them more vulnerable to the effects of cancer-causing viruses. When these damaged cells are infected with certain viruses, such as human papillomavirus (HPV), they can become cancerous and lead to the development of oral cancer. Additionally, heavy drinking can weaken the immune system, which can further increase the likelihood of developing oral cancer. Therefore, it’s important to be mindful of alcohol consumption habits and take steps to reduce the risk of oral cancer, such as limiting alcohol intake, practicing good oral hygiene, and getting regular dental check-ups [3, 12, 20].

**Human papillomavirus**

Infection with human papillomavirus (HPV), specifically type 16, is a recognized risk factor and causative agent for oral cancer. However, there is a growing subset of patients diagnosed with oral cancer who do not fit the traditional demographic profile. Unlike the historically high-risk groups - people over 50, African Americans, males, and tobacco users - this new population is primarily made up of non-smoking, white individuals between the ages of 30 and 50, with males slightly outnumbering females. Research suggests that HPV16 is the main risk factor for this new population. The virus is also responsible for most cervical cancers and is the most common sexually transmitted infection in the US. Oral cancer in this group typically affects the tonsils, tonsillar pillars, base of the tongue, and oropharynx. Notably, individuals who develop oral cancer from this cause tend to respond better to radiation treatment than those whose disease is caused by tobacco use [20-24].
### Table 1. Staging System

<table>
<thead>
<tr>
<th>Stage</th>
<th>Number Staging System</th>
<th>TNM System</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Pre-cancerous condition</td>
<td>-</td>
<td>High risk of developing into invasive cancer if left untreated</td>
</tr>
<tr>
<td>1</td>
<td>Early invasive cancer</td>
<td>T1N0M0</td>
<td>Tumor ≤2cm, no spread to nearby tissues, lymph nodes, or organs</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td>T1N1M0</td>
<td>Tumor &gt;2cm but ≤4cm, may have spread to nearby tissues, but not to lymph nodes or organs</td>
</tr>
<tr>
<td>3</td>
<td></td>
<td>T2N0M0</td>
<td>Tumor &gt;4cm, may have spread to lymph nodes or nearby tissues, but not to other organs</td>
</tr>
<tr>
<td>4a</td>
<td>Advanced cancer</td>
<td>T3N0M0</td>
<td>Cancer has grown into surrounding structures or spread to one lymph node ≤3cm</td>
</tr>
<tr>
<td>4b</td>
<td></td>
<td>T3N1M0</td>
<td>Cancer has spread to nearby areas like the base of the skull or surroundings of the neck arteries or has spread to a lymph node &gt;6cm</td>
</tr>
<tr>
<td>4c</td>
<td></td>
<td>T4N0M0</td>
<td>Cancer has spread to other parts of the body like the lungs or bones</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T4N1M0</td>
<td>Same as above, plus cancer has spread to at least one lymph node</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T4N2M0</td>
<td>Same as above, plus the cancer has spread to at least two lymph nodes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T4N3M0</td>
<td>Same as above, plus the cancer has spread to at least three lymph nodes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>M1</td>
<td>Cancer has spread to other parts of the body, such as the liver, brain, or distant lymph nodes</td>
</tr>
</tbody>
</table>

### Nutritional factors

Historically, clinicians have noted a connection between iron deficiency and oral squamous cell carcinoma (OSCC), and subsequent research has consistently supported this association. Iron is essential for maintaining the health and integrity of epithelial tissues, and deficiencies can result in atrophic changes in the oral epithelium, rendering it more vulnerable to chemical carcinogens. Moreover, a diet low in fruits and vegetables has been associated with an elevated risk of OSCC, whereas a higher intake of these foods seems to decrease the risk. Encouragingly, interventional trials employing β-carotene and vitamin A have yielded promising outcomes in mitigating the severity of oral precancerous lesions. It is worth noting that riboflavin deficiency, commonly encountered in individuals who consume excessive alcohol, may also play a role in the development of OSCC. In summary, addressing nutritional deficits and advocating for a well-balanced diet could significantly contribute to both the prevention and treatment of OSCC [25].

### Edentulous patients

Edentulous patients and poor oral hygiene are known risk factors for cancer of the oral cavity. Additionally, some studies suggest that the use of mouthwashes with high alcohol content may increase the risk of developing tongue and oral cavity squamous cell carcinoma (SCC), although this association remains unproven. Furthermore, research has linked the consumption of the traditional South American beverage, mate, to an elevated risk of oral cavity cancer [26].

### Ultraviolet (UV) light

The oral microbiome, mucosal inflammation, and oral mucosal trauma caused by teeth and prosthetic devices have been gaining attention as potential contributors to the development of oral cancer. In addition, exposure to actinic ultraviolet radiation (UV), particularly UV-B, has been implicated in the development of lip cancer. Genetic predispositions, such as xeroderma pigmentosum, Fanconi’s anemia, and ataxia-telangiectasia, also increase the risk of developing oral cancer due to defects in DNA repair mechanisms [26].

### Prevention

Oral cancer can be considered a largely preventable disease, given that most risk factors can be eliminated. However, it can still occur in individuals who do not belong to known risk categories. Therefore, primary prevention through education on limiting behavioral risk factors, such as tobacco use and excessive alcohol consumption, is crucial. Additionally, HPV vaccination may also play a role in prevention, although its effectiveness in preventing oral cancer is not as well established as it is for anogenital and cervical cancer. Early detection and treatment of oral premalignancies and early-stage cancers are critical components of secondary prevention. Unfortunately, despite increased public awareness, the proportion of patients presenting with advanced disease has remained relatively unchanged over the past four decades [6,8,12,22].

Unlike other common cancers such as colorectal or cervical cancer, implementing a standardized population-based screening program for oral cancer is not cost-effective and therefore cannot be recommended. This is because the incidence of oral cancer is relatively low compared to other cancers, and the cost of screening the entire population would outweigh the benefits. However, targeted screening programs in high-risk populations, such as heavy smokers and drinkers, or individuals with a history of cancer outside the head and neck region, may be worth considering. Studies have shown that such targeted approaches can help identify early-stage cancer or precancerous lesions, potentially improving treatment outcomes. For example, a randomized controlled trial conducted in India demonstrated the effectiveness of a screening program in high-risk individuals. Additionally,
opportunistic screening for oral mucosal lesions during routine dental check-ups in countries with good dental healthcare infrastructure could also contribute to reducing diagnostic delays and improving outcomes [27-30].

**Staging System**

According to the TNM staging system by the American Joint Committee on Cancer, there are four stages of oral cancer based on the tumor size, lymph nodes involved, and metastasis (Table 1) [16,31,32].

**Oral Carcinogenesis**

Oral carcinogenesis is a multifocal process involving genetic alterations in squamous epithelial cells, which can be detected through various molecular biology techniques. High-throughput methods are being used to search for oral cancer biomarkers in biofluids like saliva and serum. The concept of “field carcinization” suggests that cancer can develop at multiple sites, and research has shown that mutations in the p53 gene are linked to smoking and increase the risk of oral carcinoma. Long-term exposure to environmental and exogenous factors may lead to multi-focal presentations and mutational expressions of tumor suppressor genes, making it difficult to surgically remove premalignant lesions [33].

**Epidemiology**

It’s worth noting that these statistics are based on data from 2012, so they may not reflect current trends. Additionally, the incidence and mortality rates vary widely depending on the specific type of oral cancer, with some types having much higher incidence and mortality rates than others [34-53] (Table 2).

**Oral screening**

According to recent statistics, only a minority of oral and pharyngeal cancers, approximately 30%, are detected at an early stage, whereas 50% are diagnosed at a more advanced stage (stage III or IV) when they have already spread to other parts of the body. This delay in detection is attributed to several factors such as patients seeking medical attention too late, diagnostic delays, and the absence of well-defined guidelines for referring patients from dentists to physicians. Consequently, incorporating oral cancer screenings into regular head and neck examinations performed by primary dental care providers is crucial [54-57]. The primary screening test for oral cancer involves a thorough clinical examination of the oral cavity. As recommended by the World Health Organization and the National Institute of Dental and Craniofacial Research, this examination should consist of

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**Table 2. Oral Cancer Statistics**

<table>
<thead>
<tr>
<th>Region</th>
<th>ASIR for Oral Cancer (per 100,000 population)</th>
<th>ASMR for Oral Cancer (per 100,000 population)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Global</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Europe</td>
<td>12.1</td>
<td>7.4</td>
</tr>
<tr>
<td>North America</td>
<td>4.2</td>
<td>3.1</td>
</tr>
<tr>
<td>South America</td>
<td>7.2</td>
<td>5.4</td>
</tr>
<tr>
<td>Asia</td>
<td>10.4</td>
<td>7.4</td>
</tr>
<tr>
<td>Australia</td>
<td>6.8</td>
<td>3.9</td>
</tr>
<tr>
<td>Country-specific</td>
<td></td>
<td></td>
</tr>
<tr>
<td>United States</td>
<td>4.4</td>
<td>3.1</td>
</tr>
<tr>
<td>Canada</td>
<td>4.2</td>
<td>3.1</td>
</tr>
<tr>
<td>Mexico</td>
<td>3.1</td>
<td>2.1</td>
</tr>
<tr>
<td>India</td>
<td>9.4</td>
<td>5.5</td>
</tr>
<tr>
<td>Brazil</td>
<td>7.2</td>
<td>5.4</td>
</tr>
</tbody>
</table>

Note that this table combines the information from both systems, so it's not strictly following either system, but rather providing an overview of the different stages and their corresponding characteristics.
a systematic visual inspection of the face, neck, lips, labial mucosa, buccal mucosa, gingiva, floor of the mouth, tongue, and palate. A mouth mirror can be used to aid in visualizing all surfaces. In addition to the visual inspection, the examination should also include palpation of the regional lymph nodes, tongue, and floor of the mouth. Any abnormality that persists for more than two weeks should be re-evaluated and referred for biopsy. Early detection through regular screening can significantly improve treatment outcomes and survival rates for patients with oral cancer [58].

**Early diagnosis**

Oral cancer, which includes cancer of the lips, tongue, floor of the mouth, and other parts of the mouth, is a common type of cancer worldwide. Early detection is crucial in reducing oral cancer mortality. Most oral cancers occur in visible or palpable areas, making early diagnosis possible. Key indicators of oral cancer include ulceration, induration, infiltration, bleeding, and lymphadenopathy [55,59]. Oral cancer, which affects the mouth, tongue, lips, or throat, can be detected early through opportunistic oral cancer screening exams performed by oral health professionals (OHPs). During these exams, OHPs check for signs of cancer or precancerous changes in the mouth, and if they find anything suspicious, they refer the patient to a specialist for further evaluation. To diagnose oral cancer, a combination of clinical evaluation and biopsy is used. The biopsy is the most reliable method, involving the removal of a small tissue sample from the affected area for examination under a microscope. Imaging tests like CT scans, MRI scans, or PET scans help determine the cancer’s extent, which guides treatment decisions. For early-stage oral cancer, surgery or radiation therapy may be enough. Advanced cancers might require a combination of surgery, radiation therapy, and chemotherapy. Targeted therapy could also be combined with radiation therapy for more aggressive cases. Managing oral cancer patients requires a multidisciplinary approach to address various side effects, including infections, mucositis, oral ulceration, xerostomia, bleeding, pain, osteoradionecrosis, taste loss, trismus, and dental caries. A team of healthcare professionals can help mitigate these issues and enhance the patient’s quality of life. Early detection and prompt treatment are crucial for improving oral cancer outcomes. By performing regular opportunistic oral cancer screening exams, OHPs can identify cancer early, leading to better patient outcomes. A collaborative effort among healthcare professionals is essential for managing the diverse needs of oral cancer patients [60,61].

**Before treatment**

It is crucial for dentists to perform a thorough dental assessment and develop an oral care program before beginning cancer treatment to enhance treatment compliance and reduce infection risk. Most patients have underlying dental problems such as cavities and gum disease, so dentists must provide proper oral rehabilitation, non-invasive treatments, fluoride dental trays, and maxillofacial prosthetics when necessary. Additionally, radiation therapy can cause oral complications, and surgery may require removing infected teeth and bone resection. To prevent osteoradionecrosis, dentists should extract at-risk teeth seven to ten days before radiation therapy begins and ensure all sources of mucosal trauma are eliminated. A personalized oral hygiene regimen should also be implemented, including brushing, flossing, scaling, professional tooth cleaning, and denture cleaning [62]. Depending on the area being irradiated, provisions should be made for customized dental fluoridation trays. By following these guidelines, dentists can help protect their patients’ oral health during cancer treatment. And other diseases, such as types of cancer, respiratory diseases and Alzheimer’s, it is important to check the condition of the disease [63-67].

**Treatment**

Treatment for mouth cancer is tailored to the specific characteristics of the cancer, including its location, stage, and aggressiveness, as well as the patient’s overall health and personal preferences. Patients may receive a single type of treatment or a combination of different therapies, such as surgery, radiation, and chemotherapy. It’s essential to discuss the various options with a doctor to determine the best course of action for each individual case.

**Surgery**

Surgery has been the cornerstone of treatment for oral cancer for over a century, with a rich history dating back to the late 19th century. The advent of ionizing radiation therapy in the early 20th century revolutionized the treatment landscape, offering a non-invasive alternative to surgery. While radiation therapy remains an essential component of treatment for many patients, it is often used in combination with surgery, particularly in cases of advanced cancer. In these instances, postoperative radiation therapy is typically employed to ensure that any remaining cancer cells are eliminated and reduce the risk of recurrence [68].

**Chemotherapy**

In the past, chemotherapy was primarily used as a palliative treatment for oral carcinoma in the 1950s, 60s, and 70s. However, with the advent of cisplatin, clinical trials on induction chemotherapy showed promising results, with a considerable number of patients exhibiting responses to the treatment. Unfortunately, despite these initial positive outcomes, the use of induction chemotherapy did not lead to long-term control of primary oral squamous cell carcinomas, unlike its effectiveness in other head and neck tumors [69].

**Targeted drug therapy and Immunotherapy**

Researchers are actively exploring targeted therapies that focus on inhibiting epidermal growth factor receptor (EGFR) as a potential treatment for non-small cell lung cancer. In addition, immunotherapy and gene therapy are other promising areas of study that require further investigation. These approaches have shown encouraging results in early clinical trials, and scientists are working to
optimize their use in combination with existing treatments or as standalone therapies. The ultimate goal is to develop more effective and personalized treatments that can improve patient outcomes and quality of life [68,70].

In conclusion, early detection of oral cancer is crucial for improving treatment outcomes and saving lives. With advancements in technology and medical research, various diagnostic tools and techniques are available to aid clinicians in identifying and diagnosing oral cancer at its earliest stages. These include visual examination devices, salivary biomarker tests, and other point-of-care testing methods that can help identify potential cancerous lesions before they progress to advanced stages. While surgical biopsy and histology remain the gold standard for definitive diagnosis, these auxiliary methods can provide valuable information to support clinical decision-making. The scientific community continues to make strides in developing novel approaches to prevention, screening, and early detection of oral cancer. By staying up-to-date with the latest research and incorporating cutting-edge technologies into their practice, healthcare professionals can significantly reduce diagnostic delays and improve patient outcomes. In turn, this will lead to better management of oral cancer and improved quality of life for patients.

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Data availability

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Approved by any scientific Body

Not applicable as the manuscript is not a part of any student thesis or study.

Ethical issue and approval

Not applicable as we used information from previously published articles.

Consent for publication

All authors have given consent for publication.

Conflict of interest

The authors declare no potential conflict of interest.

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