

The Current Scenario Regarding the Narrative Advancement of Oral Cancer

Abstract

Oral cancer is one of the most common types of cancer, and it is a big health issue, especially in developing countries. Even though science has come a long way in various ways, it is still one of the leading causes of death. In many developing countries, smoking and drinking alcohol seem to be the main things that cause oral cancer. Oral cancer (OC) is the most common type of cancer in India. It causes 50–70% of all cancer deaths and has the highest rate of occurrence among Asian countries. Most of the time, oral cancer affects the front of the tongue, the cheek, the floor of the mouth, the gums, or any other part of the mouth, including the palate, the lip, and the floor of the mouth. There are a lot of differences in how often oral cancer happens around the world. The biggest cause of oral disease-related deaths worldwide is estimated to be oral cancer, which is a serious health concern.

Keywords: Oral cancer, Oropharyngeal cancer, Oral squamous cell carcinoma

Introduction

Oral cancer is a malignant neoplasia that starts in the mouth or on the lip. Oral cancer is also known as oral squamous cell carcinoma since 90% of malignancies in the dental region start in the squamous cell layer (OSCC). It is more likely to spread to lymph nodes and has different levels of differentiation.^[1] Oral cancer is still a big problem for public health. It affects men, women, and people of all races around the world. The average age is around 60, but more and more people in younger age groups are getting it these days. The sixth most prevalent form of cancer in people is oral cancer. 48% of persons with head and neck cancer are affected by it. 90% of oral cancer cases that are examined under a microscope are oral squamous cell carcinomas (OSCC). Even if there are more effective and new approaches to detect oral cancer, the survival rate is still around 50% in the majority of nations.^[2,3] Oral cancer is a multifactorial lesion. Most oral cancers are found in people who smoke a lot, drink too much, or use different kinds of tobacco regularly or often in a day. Oral cancer can also be brought on by long-term inflammation, ultraviolet (UV) radiation (for lip cancer), human papillomavirus (HPV) or Candida infections, immunosuppression, genetic predisposition, and nutrition. Most of the time, using tobacco in different ways and

drinking alcohol are the main things that put you at risk for developing cancerous lesions in the mouth.^[4] Oral cancer can show up in many different ways, which can make it hard to spot early on because some of the symptoms are the same as those of benign lesions.^[5]

Stage determination of cancer

The extent of an oral cavity or oropharyngeal cancer is determined by "staging" the condition once it has been discovered and its size and spread have been established.^[6] Oropharyngeal and oral cavity tumors are often staged using the TNM method developed by the American Joint Committee on Cancer (AJCC). This system is founded on three crucial bits of knowledge:^[7,8]

- The extent (T) of the tumor: How big is the primary tumor, and has it spread to any other oral or throat tissues?
- Has the disease reached surrounding lymph nodes (N): Has the malignancy spread to nearby lymph nodes? If so, how many are located on the side where the cancer first appeared and how big are they?
- Has cancer metastasized, or spread to distant locations, to other body organs like the lungs?.

Based on the size of the primary tumor (T), whether or not it has migrated to adjacent lymph nodes (N), and whether or not it has

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moved to other areas of the body (M), the TNM method is used to stage cancer (M). The numbers show the tumor's size relative to the body as a whole. You can learn more about each of these things from the numbers or letters that come following T, N, and M. The cancer is further along if the number is higher. Once a person's T, N, and M categories have been figured out, they are put together in a process called "stage grouping" to figure out their overall stage (**Table 1**).

Stage 0 is the first stage of cancer in the mouth, throat, or oropharynx (carcinoma in situ). Then, the stages go from I to IV. In general, the number shows how far cancer has spread. When the number is higher, like in stage IV, it means that cancer has spread more. And within a stage, a letter that comes earlier is a sign of a lower stage. Even though everyone's cancer is different, cancers at the same stage often have the same outlook and are often treated similarly.^[9, 10]

Typically, oral cancer develops on the lower lip (in 10% of cases), the floor of the mouth (30%), and the ventral-lateral border of the tongue (in 40% of cases). Despite how simple it is to check inside the mouth during a clinical examination, oral cancer is typically discovered when it is too advanced. The most frequent causes of this are an incorrect initial diagnosis and a lack of understanding on the part of the patient or the person providing care, both of which reduce the likelihood that the patient will survive despite therapy.

Table 1. TNM Definitions for Oral Cancer^[11-13]

Primary tumor (T)	
TX	Cannot be assessed
T0	No evidence of primary tumor
Tis	Carcinoma in situ (CIS)
T1	Tumor 2 cm or less in greatest dimension
T2	Tumor more than 2 cm but not more than 4 cm in greatest dimension
T3	Tumor more than 4 cm in greatest dimension
	Moderately advanced local disease. Lip: Tumor invades through cortical bone, inferior alveolar nerve, the floor of mouth, or skin (chin or nose).
T4a	Oral cavity: Tumor invades through cortical bone, into deep/extrinsic muscle of tongue (genioglossus, hyoglossus, palatoglossus, and styloglossus), maxillary sinus, or skin of the face.
	Very advanced local disease. Lip and oral cavity: Tumor invade
T4b	masticator space, pterygoid plates, or skull base; or encases internal carotid artery
Regional lymph nodes (N)	
NX	Cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in a single ipsilateral lymph node, 3 cm or less in the greatest dimension

Cancer staging can be complex.

The prognosis for oropharyngeal tumors with HPV DNA present (referred to as p16-positive) is typically better than for

those without HPV (p16-negative). Separate staging systems are utilized because p16-positive tumours have a better prognosis than p16-negative oropharyngeal malignancies.

Recurrent (relapsed) cancer

This is not a real stage in the TNM system. Cancer that returns after therapy is referred to as recurrent or relapsed cancer. Recurrent oral or oropharyngeal cancer can spread to other organs like the lungs or arise locally in the mouth or throat, regionally in close-by lymph nodes (distant recurrence).^[14]

The body might suffer from oropharyngeal cancer in many different places. The walls of the pharynx, the tonsils, the bottom of the tongue, and the underside of the soft palate are where it occurs most frequently. Despite being two distinct illnesses, oral cancer and oropharyngeal cancer share several risk factors, such as smoking and drinking. Human papillomavirus high-risk strains are presently thought to be the primary cause of over 70% of oropharyngeal cancers (HPV). Cancers of the lip, tongue, gums, mouth floor, palate, and other oral structures are included in the category of oral cancer.

Mortality^[15]

Most countries have death rates that are too high—around 50 percent—except for a few places that stand out. This hadn't changed in a long time, even after better ways of diagnosing problems and more recent improvements in surgery.

Demography

Age and sex, socioeconomic status, ethnicity

Age and sex: Men's rates were 7 times greater than women's decades ago. Global incidence rates indicate obvious gender inequalities.^[16] Men are more likely to smoke and drink, but the ratio is dropping in countries where women do the same. Most oral cancer patients are 50 or older. The average age is 60-65 (the mean age is 62). In the late 20th century, mouth cancer became increasingly common in those under 45, and this trend continues.^[17]

Socioeconomic status: Oral cancer rates are highest in low-income and resource-poor areas. Conway *et al.* found the same evidence whether measured by income, education, or occupation and even when other important risk variables were considered. Men are more connected than women.^[18]

Ethnicity: Oral cancer incidence and mortality vary greatly by ancestry and ethnicity. These variations are generated by dangerous cultural practices. Chewing betel quid increases the risk of mouth cancer. South, East, and Melanesia are affected. There are variances within the same country. Oral cancer is more common among Indians in Malaysia than Malays or Chinese. More colored than black Africans acquire mouth cancer in South Africa. Black males are more likely to have oral cancer than white or Hispanic men, according to studies. Social and environmental factors may cause these variances. Blacks tend to get oropharyngeal cancer later than whites. Oral cancer is far more common among South Asian immigrants in

the UK than among natives. India is responsible for one-fourth of all cases worldwide, with 77,000 new cases and 52,000 fatalities per year. Oral cancer is a significant public health concern in India due to its high prevalence. 70% of mouth cancer cases in India are identified after they have progressed, as opposed to 30% in the West (American Joint Committee on Cancer, Stage III-IV). If identified too late, recovery chances are nearly nonexistent. 20% of people survive after five years.^[19]

Trends

Reports say that the number of people getting lip cancer is going down in several countries where it used to be common. Changes in the world's population are thought to make the number of new cases of oral cancer rise by 62 percent, to 856,000 per year, by 2035. In the United Kingdom, the number of people who get oral cancer and die from it has gone up by 35%, which is a big deal. This increase has happened more quickly among young adults. In some places, more and more people are getting tongue cancer.^[20, 21]

Young people^[22]

In the West and Australia, 4-6% of oral cancer cases are now discovered in patients under the age of 45, and rates in Asia may be higher. The largest case series of young people with oral cancer done to date in Europe was included in our research, which were conducted in Southern England. One-fourth of the cases in our study lacked any established risk factors, and a large number of them came from professional classes.

Risk factors^[23-25]

Oral cancer is the world's sixth most common type of cancer. Oral cancer is a big problem in Southeast Asia, mostly because people there tend to chew betel nuts, smoke, and drink a lot of alcohol. Several things that put people at risk caused oral cancer.

People who regularly use both cigarettes and alcohol are at much greater risk, especially when both are consumed in considerable amounts (**Table 2**).

- ✓ Infection with the human papillomavirus (HPV) is another risk factor.
- ✓ Repeated sun exposure to the face
- ✓ Prior oral cancer diagnosis
- ✓ History of oral or other cancers in the family
- ✓ Compromised immune system.
- ✓ Poor dietary habits
- ✓ Gene-related syndromes
- ✓ Mate consumption
- ✓ Consistent trauma
- ✓ Bacterial infections
- ✓ Dental aspects
- ✓ Workplace hazards
- ✓ Syphilis
- ✓ Being a man

Oral cancer strikes men twice as frequently as it strikes women.

Oral cancer types

Cancer of the squamous cell

More than 90% of cancers of the oral cavity are squamous cell carcinomas. Squamous cells, which are flat and superficially resemble fish scales, border the throat and mouth in normal circumstances. When some squamous cells mutate and become aberrant, squamous cell cancer develops.^[26]

Rarer forms of oral cancer

- Verrucous carcinoma
- Minor salivary gland carcinomas
- Lymphoma

Conditions that could be precancerous

Benign tumors of the oral cavity: The oropharynx and oral cavity can both produce a variety of benign tumors, both malignant and not. These can occasionally progress to oral malignant cancer. For this reason, benign tumors are often surgically removed. These benign lesions include Granular cell tumor, Keratoacanthoma, Verruciform xanthoma, Papilloma, Fibroma, Schwannoma, Eosinophilic granuloma, Keratoacanthoma, Granular cell tumor, Lipoma, Condyloma acuminatum, Neurofibroma, Osteochondroma and Leiomyoma.

These non-cancerous disorders, leucoplakia^[27] and erythroplakia, appear when specific types of aberrant cells proliferate in the mouth or throat. Leucoplakia manifests as a white patch, but erythroplakia manifests as a red spot that may be flat or slightly elevated and frequently bleeds when scraped. Both disorders have the potential to progress into different types of cancer since they are precancerous. To find out if the cells are malignant when these criteria exist, a biopsy or other test is carried out. A quarter of leucoplakias are either precancerous or develop into malignancy when they are first found. Approximately 70% of instances of erythroplakia are thought to be malignant, either at the time of diagnosis or afterwards. This makes them generally more dangerous.

Types of oral cancer by region^[28]

Any area of the mouth, including the lips, gums, tongue, roof of the mouth, cheeks, and uvula, can develop mouth cancer.

Types of oral cancer include:

- Lip cancer
- Jaw cancer
- Palate, cheek, and other mouth cancers

The CDC reports that cancer instances have been discovered in several oral regions:

- Floor of the mouth
- Gum
- Soft palate and uvula
- Hard palate
- Cheek and other mouths

Advanced stages of oral squamous cell carcinoma

Advanced-stage OSCC is defined by the presence of tumors measuring over 4 cm in size or infiltrating neighboring structures. These stages of the disease manifest as extensive ulcerated zones with important in-depth infiltration or as exophytic growths with a notorious verrucous component. Advanced-stage OSCC is associated with constant pain, with the need for frequent doses of analgesic medication. Narcotic agents are commonly required to control the pain, which irradiates toward neighboring structures such as the parietal zone, the ear, or in-depth areas.^[29]

Other OSCC subtypes

Numerous OSCC forms or subtypes have been identified, including basaloid squamous cell carcinoma (SCC), spindle cell squamous cell carcinoma (SCC), adenosquamous cell carcinoma (SCC), carcinoma cuniculatum, verrucous SCC, lymphoepithelial carcinoma, papillary SCC, and acantholytic SCC.

Other malignant tumors of the oral epithelium

Ackerman's Verrucous Carcinoma
Melanoma

Oral squamous cell carcinoma, the most common type of oral cancer, is characterized by a variety of erythroleukoplakic lesions, exophytic tumors, or small ulcerations. The differential diagnosis is established with the following disease conditions that may resemble a squamous cell carcinoma in its clinical appearance.

- Traumatic Ulcerations
- Erythroleukoplakia
- Median Rhomboid Glossitis
- Eosinophilic Granuloma
- Keratoacanthoma (KA)
- Necrotizing Sialometaplasia (NSM)
- Benign Tumors
- Infectious Processes

Common oral cancer symptoms

The signs and symptoms of mouth cancer are comparable to those of other types of oral cancer. These signs are frequently misdiagnosed as a lingering cold or an ongoing mouth sore. Other signs of oral cancer may include:

- Sore on lip or mouth that won't heal
- Lump or growth anywhere in mouth
- Bleeding mouth
- Missing teeth
- Discomfort swallowing
- Difficulty in wearing dentures
- Lump in neck
- An earache that is persistent
- Significant weight reduction
- Numbness in chin, neck, lower lip or face
- White, red and white or red patches in the hard palate and lips
- Sore throat

- Jaw discomfort or stiffness
- Pain in tongue^[30-33]

Cancer screening, early detection

Numerous traditional diagnostic methods are frequently employed to find oral cancer. Early cancer detection allows for more effective treatment. The morbidity and mortality associated with cancer are impacted by diagnosis delays. As a result, early clinical diagnosis and screening enable the delivery of more safe and affordable medicines. Early diagnosis is significantly impacted by public awareness of healthcare professionals. Dental professionals must be aware of the value of screening for pre-malignant and malignant lesions in the mouth. Dentists typically perform the initial examination of the oral cavity, giving them the opportunity to check for oral cancer. A prominent precancerous lesion helps doctors identify and treat patients early.

An more method to detect oral cancer early is to self-examine your mouth. Salivary biomarkers are diagnostic tools for possibly cancerous and benign disorders of the mouth. For instance, saliva from OSCC patients has significantly higher levels of the cancer antigen CA-125, the tissue polypeptide antigen [TPA], and the tumor marker Cyfra-21-1. Choline and pipercolate can be discovered in OSCC patients' saliva even in the earliest stages. The best diagnostic approach is a result of experience and education working together. Salivary indicators make it feasible to diagnose oral cancer early. There are several techniques that can be used to recognize pre-malignant and malignant lesions of the oral cavity, including toluidine blue staining and Lugol staining. The gold standard for diagnosing oral cancer should still be tissue samples and histological examination. The incidence of OPSCC in women is declining in the United States due to increased preventative healthcare, including screening, which is similar to the trend for cervical cancer. Additionally, one or more of the subsequent tests could be performed.^[34-36]

- X-rays to check for the spread of cancer cells to the jaw, chest or lungs.
- CT scan to detect any cancers in neck, lungs, mouth, throat or any other parts of the body.
- PET scan in order to identify whether the cancer has spread to the lymph nodes or other organs.
- MRI scan to provide a clearer picture of the head and neck and assess the cancer's stage or extent.
- Endoscope to check the trachea, windpipe, inner throat, sinuses and nasal passages.
- A physical examination of the mouth region to check for cancerous growths and a swab to collect cells for laboratory testing are required for diagnosis.

Biomarkers^[37, 38]

The National Cancer Institute defines a biomarker as "a biological molecule discovered in blood, other body fluids, or tissues that is a sign of a normal or aberrant process, of a state, or of a disease," like cancer. A patient with the condition can frequently be distinguished from a healthy person using biomarkers. Genomic, proteomic, and metabolomic are some generic terms for biomarkers. The main objectives of research

on oral cancer biomarkers in molecular biology and oncology are finding significant biological molecules or markers that may be linked to cancer development, risk assessment, screening, recurrence prediction, indicating prognosis, indicating invasion/metastasis, and tracking therapeutic responses of cancer. A salivary biomarker called Cluster of Differentiation Factor 34 can forecast the likelihood of oral squamous cell carcinoma recurrence (OSCC). Genomic markers such as integrin-3 and integrin-4 can help determine if malignant oral squamous cells will spread locally and hematogenously. Additional examples of genetic markers used to predict radio-resistance in OSCC tissue include B-cell lymphoma-2, claudin 4, yes-associated protein 1, MET proto-oncogene, and receptor tyrosine kinase.

The role of anti-inflammatory drugs on cancer prevention^[39]

Celecoxib (CXB) is licensed for early cancer prevention in familial adenomatous polyposis. CXB has anti-angiogenesis, anti-EMT, and other anti-cancer molecular pathways. CXB suppressed OSCC EMT in murine models. Aspirin decreases colorectal cancer risk. A recent study on aspirin and head and neck cancer indicated a reduced risk in persons with low to moderate cigarette smoke or alcohol usage. Aspirin enhanced survival in head and neck cancer patients, according to another study. Recent research found no effect of aspirin on HNSCC survival or recurrence.

Common treatments for mouth cancer include:^[40, 41]

- **Surgery:** A treatment called tumor resection involves entirely removing the mouth tumor. Depending on where the tumor is located, a little incision may be made in the jawbone or neck to make removal easier. After a tumor is surgically removed, a portion of the mouth might need to be rebuilt. In certain cases, our surgeons may do pedicle or free flap reconstruction.
- **Radiation therapy:** Modern radiation therapy technology uses equipment developed to spare healthy tissue and speed up procedures to more precisely treat malignant tissues of the mouth. The two most often utilized radiation therapies for treating oral cancers are external beam radiation therapy (EBRT) and brachytherapy.
- **Chemotherapy:** Using medications to eradicate cancer cells throughout the body, chemotherapy is sometimes paired with radiation therapy. To combat cancer cells at various stages of their growth cycles and reduce the likelihood of drug resistance, several chemotherapeutic medicines may be combined.
- **Targeted drug therapy:** Targeted drug therapy inhibits the molecular growth of cancer cells. In a tailored treatment strategy for oral cancer, it may be used with chemotherapy and/or radiation therapy.
- **Immunotherapy:** These drugs help the body's immune system find and get rid of cancer cells. Immunotherapy can be used to treat cancers of the mouth and oropharynx. Drugs are used in immunotherapy to boost a person's immune system so it can find and destroy cancer cells more effectively. To improve the immunological

response, it frequently targets particular immune system proteins. Compared to chemotherapy, it has distinct (and occasionally less negative) side effects. Some immunotherapy medications, such as monoclonal antibodies, have many mechanisms of action against cancer cells and may also be referred to as targeted drug therapy because they prevent the growth of the cancer cell by blocking a particular protein on the cancer cell.

Outlook

The type and stage of cancer at the time of diagnosis affect the prognosis for oral malignancies. Additionally, it is influenced by overall health, age, tolerance, and treatment response. Early detection is essential because cancer treatments may be more effective and involve fewer complications.

Table 2. Summary of risk factors and prevention strategies for oral cancer

Risk factors	Prevention strategies
Tobacco, smokeless tobacco ^[42-44]	Probiotics ^[45]
Alcohol consumption	Chemoprevention
HPV infection ^[46-48]	Anti-inflammatory drugs
Inflammation	Cancer screening
Oral microbiome ^[49, 50]	Early detection
Genetic predisposition	Using biomarkers

Conclusion

In recent decades, we've made great strides in understanding the etiology, biology, and molecular underpinnings of oral cancer, as well as in diagnosing and treating it. Since the 1970s, oral cancer—particularly tongue cancer—has increased in many countries, and recent research show that oropharyngeal cancer has been steadily increasing in high-income nations. Over 750 papers have been written on this subject since the World Health Organization classified oral potentially malignant diseases (OPMDs) in 2007. The investigation that came before it demonstrates that eating betel nut and smoking tobacco are significant mouth cancer risk factors. Despite avoiding lifestyle or environmental risk factors, many people are diagnosed with mouth cancer. Genetic susceptibility is likely to play a role. The public and physicians should be aware of the risk factors for oral cancer, and dentists should search for early indicators of oral cancer during routine exams, especially in patients with established risk factors.

Risk factors, early detection, and cancer treatments have been studied extensively. Oral cancer has substantial morbidity and fatality rates, requiring more effective techniques and treatments. Oral cancer patients usually undergo surgery. Patients who can't tolerate surgery receive radiotherapy and chemotherapy. All of the above treatments cause emotional and physical issues. Preventing and detecting oral cancer early can decrease these effects. Probiotics and natural products may prevent and treat oral cancer, but further research is needed. Awareness of risk factors and early indicators of oral cancer impacts prevention.

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Conflict of interest

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Ethics statement

None.

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