

## ***Oral Cancer***

Oral cancer is a term used for general description of malignant tumors of the oral cavity. Over 94% of oral cancers are squamous cell carcinoma (SCC).

Oral squamous cell carcinoma (oscc) is a malignant neoplasm of stratified squamous epithelium that is capable of locally destructive growth and distant metastasis. OSCC is often begins as epithelial dysplasia and progressing until the dysplastic epithelial cells reach the basement membrane and invade into the underlying connective tissue.

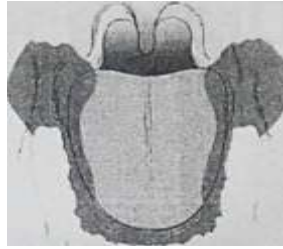
OSCC most commonly occurs in middle-aged and older individuals, although a disturbing number of these malignancies also being documented in younger adults

From an epidemiological and clinicopathological perspective, OSCC can be divided into three categories:

- carcinomas of the oral cavity proper,
- carcinomas of the lip vermilion
- carcinomas arising in the oropharynx.

Intraoral and oropharyngeal tumors are more common among men than women, with a male: female ratio of over 2:1.

In the oral cavity, the majority of cancers are concentrated in the lower part of the mouth, particularly the lateral borders of the tongue, the adjacent floor of the mouth and lingual aspect of the alveolar margin, forming a U-shaped area extending back towards the oropharynx. Two major factors help to explain why this region is at such a high risk: first, any carcinogen may mix with saliva, pool in the floor of the mouth, and constantly bathe these anatomic sites; second, these regions of the mouth are covered by a thin, non-keratinized mucosa which provides less protection from carcinogens.



Less frequently, the gingiva and alveolar ridge area is the site of origin. The buccal mucosa especially above the occlusal line is seldom involved. Compared with other intra oral sites, carcinomas arising on the hard palate and dorsum of the tongue are relatively rare.

Over 90% of malignant neoplasms (cancers) of the mouth are squamous cell carcinomas arising from mucosal epithelium the remainder are adenocarcinomas of minor salivary glands, few are undifferentiated or metastases.

Oral cancer is age related. 98% of patients are over 40. It is considerably more common in males than females.

***Etiologic factors:***

- 1- Tobacco: Tobacco is considered the most potent risk factor for oral cancer . Epidemiological studies showed that, the risk of developing oral cancer is five to nine times greater for smokers than for nonsmokers, and this risk may increase to as much as 17 times greater for extremely heavy smokers of 80 or more cigarettes per day
- 2- Alcohol
- 3- Betel quid habits
- 4- Sunlight exposure (Lip only)
- 5- Infections:
  - Syphilis (Syphilitic Leukoplakia)
  - Oncogenic Viruses (Human papilloma virus HPV16)
  - Chronic hyperplastic candidosis
- 6- Vitamin A deficiency
- 7- Iron deficiency (in severe chronic form known as Plummer-Vinson or Paterson — Kelly syndrome)
- 8- Mucosal diseases:

Oral epithelial dysplasia

Lichen planus

Submucous fibrosis

9- Genetic disorders

10- Immunosuppression: AIDS or patients on immunosuppressive therapy for organ transplantation or malignancy are at increased risk of oral squamous cell carcinoma.

***Oncogenes and Tumor-suppressor genes:***

Oncogenes and tumor suppressor genes are chromosomal components capable of being acted on by a variety of causative factors.

Normal agents or **protooncogene**, are transformed into activated oncogenes in certain malignancies through the actions of viruses, irradiation or chemical carcinogens. Once oncogenes are activated, they may stimulate the production of an excessive amount of new genetic material through amplification or overexpression of the involved gene.

Oncogenes probably involved in the initiation and progression of wide variety of neoplasms including oral squamous cell carcinoma.

Tumor suppressor genes on the other hand, allow tumor production indirectly when they become inactivated or mutated.

Genetic aberrations commonly identified in oral squamous cell carcinoma including: **myc** and (**EGFR**) epidermal growth factor receptor oncogenes. The **p53**, **p16** tumor suppressor genes. The accumulation of several of these genetic aberrations is necessary before the affected cell express a malignant phenotype.

***Clinical features:*** it is presented clinically as either:

- Leukoplakia (White patch)
- Erythroplakia (Red patch)
- Exophytic growth (mass forming fungating, papillary, verruciform)
- Endophytic indurated ulcer (Invasive, ulcerated)
- Erythroleukoplakic (combined red & white patch)



***Carcinoma of the Lip:*** Accounts for 25%-30% of all oral cancers. Carcinoma of the lower lip is far more common than the upper lip. UV light & pipe smoking are the most common cause for carcinoma of lower lip. The growth rate is slower in lower lip. The prognosis is generally favorable with over 90% of patients alive after 5 years. Lesions arise on the vermilion appears as chronic non-healing ulcer or as exophytic lesion that is occasionally verrucous in shape. Deep invasion generally appears later in the course of the disease. Metastasis to local submental or submandibular lymph nodes is uncommon but is more likely with large poorly differentiated lesions.

***Carcinoma of the Tongue:*** Squamous cell carcinoma of the tongue is the most common intra oral malignancy. Excluding lip lesions, it accounts for between 25% & 40% of oral carcinomas. It has a definite predilection to men in six-eighth decades. It is presented either, indurated non-healing ulcer, red or white lesion or speckled white lesion. Most erythroplakic patches on the tongue either carcinoma in situ or invasive squamous cell carcinoma at the time of discovery. The most common location of cancer of the tongue is the posterior-lateral border. Lesions very uncommonly develop on dorsum & tip of the tongue. Metastasis from tongue cancer is relatively common at the time of primary treatment. In general deposits from squamous cell carcinoma of the tongue are found in the lymph nodes of the neck usually ipsilateral side. The first node to be involved are submandibular & jugulodiaphragmatic nodes at the angle of the mandible.

***Carcinoma of the Floor of the Mouth:*** The floor of the mouth is the second most common intraoral location of squamous cell carcinoma, it accounts for 10-20% of cases. It occurs predominantly in older men. The usual clinical appearance is that painless non-healing indurated ulcer. It may also appear as white or red patch. The lesion may infiltrate the soft tissue of the floor of mouth, causing

decrease mobility of the tongue. Metastasis to submandibular lymph node is not uncommon.

***Carcinoma of the Buccal Mucosa and Gingiva:*** It accounts for 10% of oral squamous cell carcinoma cases. Mostly affect old males. The presenting clinical appearance varies from a white patch to a non-healing ulcer to an exophytic lesion. In the exophytic lesion is the clinical pathologic entity of verrucous carcinoma. This type sometimes associated with the use of smokeless tobacco, presents as broad based warty-like mass. It is slowly growing and very well differentiated, rarely metastasizes and has a favorable prognosis.

***Carcinoma of the Palate:*** In the soft palate, squamous cell carcinoma is common occurrence accounting for 10-20% of intraoral lesions. In the hard palate, it is relatively rare. By contrast, salivary gland adenocarcinoma is relatively common in the palate, however palatal carcinomas are commonly occurring in India where reverse smoking is common. Palatal squamous cell carcinomas present as red or white plaques or as ulcerated and keratotic masses.

### ***Clinical staging:***

Tumor size, extent of metastatic spread of oral squamous cell carcinoma are the best indicators of the patient prognosis. Quantifying these clinical parameters is called staging. The most popular staging system is:

Tumor-Node-Metastasis (TNM) system. This depend on three basic clinical features:

*T=Size of the primary tumor in centimeters*

*N=involvement of the local lymph nodes*

*M= Distant metastasis*

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### ***TNM staging system for ossc***

#### **Prima tumor size (T)**

Tx No available information on primary tumor

TO No evidence of primary tumor

Tis Only carcinoma in situ at primary site

- T1 Tumor 2cm or less in greatest diameter
- T2 Tumor more than 2cm but not more than 4cm in greatest diameter
- T3 Tumor more than 4 cm in greatest diameter
- T4a (lip) Tumor invades through cortical bone, inferior alveolar nerve, floor of mouth, or skin of face (i.e. chin, nose). Tumor is resectable.
- T4a (Oral cavity) Tumor invades through cortical bone ,into deep extrinsic tongue muscles (genioglossus, hypoglossus, palatoglossus, and styloglossus), Maxilla sinus, or skin of face, Tumor is resectable
- T4b Tumor involves masticator space, pterygoidplates, or skull base ard/or encase internal carotid artery. Tumor is unresectable.

**Regional lymph node(N) involvement**

- Nx Nodes could not be or were not assessed.
- NO No regional lymph node metastasis
- N1 Metastasis in a single ipsilateral node 3cm or less in greatest diameter
- N2a Metastasis in single ipsilateral node more than 3cm but not greater than 6cm
- N2b Metastasis in multiple ipsilateral node, none more than 6 cm in greatest diameter
- N2c Metastasis in bilateral or contralateral node, none more than 6cm
- N3 Metastasis in a node more than 6cm in greatest diameter

**Involvement by distant metastasis (M)**

- Mx Distant metastasis was not assessed
- MO No evidence of distant metastasis
- MI Distant metastasis is present

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### ***TNM clinical staging categories for oscc***

Stage I      T1N0M0

Stage II     T2N0M0

Stage III    T3N0M0, or T1, T2, or T3N1M0

Stage IV

IVA      T4aN0 or N1M0, or T1, T2, T3, or T4a N2 M0

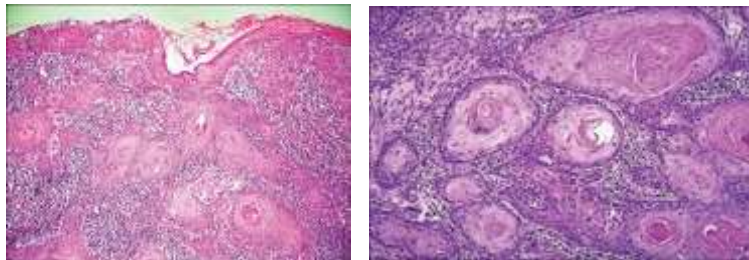
IVB      Any T N3 M0, or T4b any N M0

IVC      Any M1 lesion

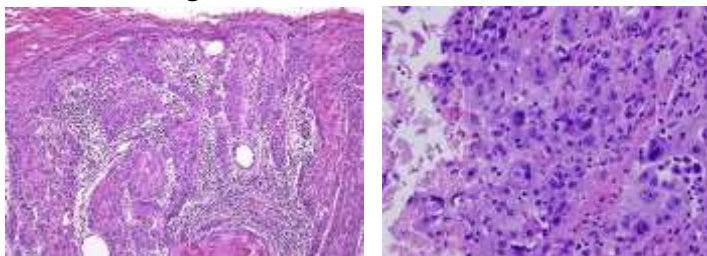
### ***Histopathology:***

Histopathological evaluation of the degree to which this tumor resemble the parent tissue (squamous epithelium) produce the normal product (keratin) is called grading. Lesion are graded on grade I-III scale.

- 1- *Well differentiated squamous cell carcinoma (grade I)*: The tumor that is closely resemble its tissue of origin & mature enough to produce keratin pearls individual cell keratinization, grow slowly & metastasize later in its course is called.

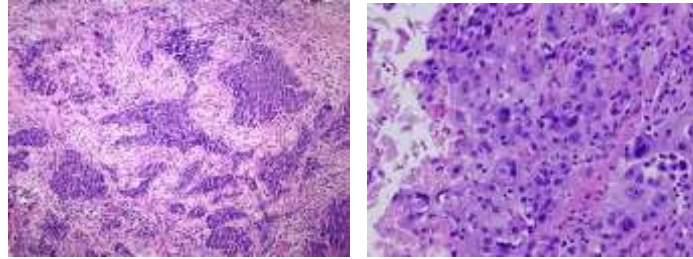


- 2- *Moderately differentiated carcinoma (grade II)*: A tumor with microscopic appearance between these grade I & II.



- 3- *Poorly differentiated squamous cell carcinoma (grade III)*: A tumor with much cellular & nuclear pleomorphism & with little or no keratin production

may be so immature that it becomes difficult to identify of tissue of origin. Such a tumor often enlarges rapidly, metastasizes early in its course.



A significant inflammatory host response is usually found surrounding the nests of invading cells. Lymphocytes, plasma cells & macrophages may all be seen in large numbers.

## **Treatment**

The treatment of intraoral squamous cell carcinoma consists of wide surgical (radical) excision, radiation therapy or a combination of surgery & radiation therapy. A variety of chemotherapeutic agents are used as adjunctive therapy.

### ***Prognosis of oral squamous cell carcinoma:***

It is generally accepted that prognosis is best in early carcinomas, especially those that are well-differentiated and not metastasized; unfortunately, most OSCC are diagnosed at late stage of disease. The prognosis of OSCC varies on a number of factors that are related to the tumor, to the treatment, and to the patient.

### ***Squamous cell carcinoma variants:***

- Verrucous carcinoma.
- Spindle cell (Sarcomatoid) Carcinoma.
- Basaloid Squamous Cell Carcinoma.
- Adenosquamous Carcinoma.

### ***Verrucous Carcinoma:***

- Low grade variant of OSSC.
- It represents 1%-10% of OSSC.

Predilection of this tumor for the buccal mucosa, lower vestibule, tongue and gingival. It's of indolent course, characterized by the rarity of metastases and the distinctive gross and microscopic pattern.



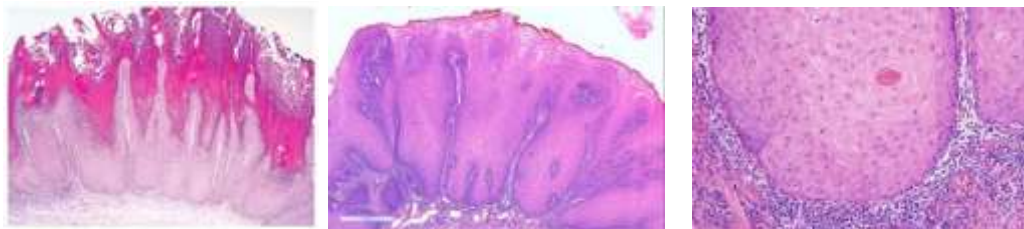
The majority of the patients were elderly men older than 55y; many had extremely poor oral hygiene or poorly fitting dentures and more than half of patients with lesions of the buccal mucosa were tobacco chewers

The macroscopic appearance of verrucous carcinoma depends on several factors like: duration of lesion, degree of keratinization and the changes in adjacent mucosa.

**Clinically:** verrucous carcinoma in the oral is characterized by painless, diffuse or well demarcated thick plaque with a cauliflower-like papillary or verruciform exophytic growth.

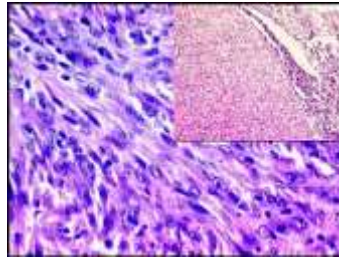


**Histopathologically:** verrucous carcinomas characterized by very well differentiated epithelial cells that appear more hyperplastic than neoplastic. it consists of thickened club shaped projections lined with thick, well-differentiated squamous epithelium with marked surface keratinization. Parakeratin typically fills the numerous clefts or crypts (parakeratin plugs) between the surface projections. The squamous epithelial cells in verrucous carcinomas are large and lack the usual criteria of malignancy. A key feature is the invasive nature of the lesion in the form of broad, pushing margins & it is surrounded by lymphocytes, plasma cells & macrophages.



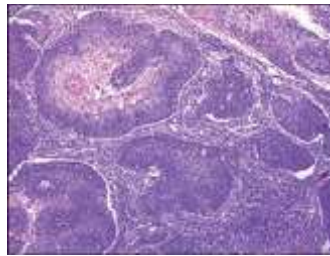
### ***Spindle cell carcinoma:***

Rarely, oral squamous cell carcinoma appears as a proliferation of spindle cells that may be mistaken with a sarcoma. Arises from the surface epithelium of the lower lip, lateral posterior tongue and alveolar ridges. Pain, paresthesia are prominent features. The tumor grows rapidly, tends to metastasize early and typically diagnosed at late stage.



### ***Basaloid Squamous Cell Carcinoma:***

Is a lesion found primarily in the upper aerodigestive tract mucosa and represents the most recently described variant of squamous cell carcinoma. It has a tendency to develop in the hypopharynx, but dozens of oral lesions have been reported.



### ***Adenosquamous Carcinoma:***

Is a rare variant of squamous cell carcinoma that is characterized histopathologically by a combination of adenocarcinoma and squamous cell carcinoma. The adenoid (glandular) pattern, which includes mucus production, has been demonstrated clearly in metastatic deposits. Some authorities consider this carcinoma to be merely a high-grade mucoepidermoid carcinoma.

