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TRADITIONAL MEDICINE TREATMENT ON ORAL CANCER

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ABSTRACT : Oral cavity cancers are part of the upper aerodigestive tract cancers and represent a significant burden worldwide. Its epidemiology varies from country to country with high frequencies in South East Asian countries. Tobacco and alcohol are the main risk factors. Survival of oral cancer is low i.e., less than 40% in the advanced stage (stage III and IV), diagnosis of oral cavity cancer is based on a complete clinical examination of the oral cavity complete with biopsy, bio-markers are an adjunct to screening and diagnosis of oral cavity cancers, surgery, radiotherapy, chemotherapy and immunotherapy are part of the therapeutic armamentarium of oral cancer but also have limitations. Traditional medicine is an important and proven alternative in the treatment and support of patients with oral cavity cancer. Prevention of oral cavity cancers includes not only early detection of precancerous and cancerous lesions but also control of risk factors and education of the population. Surgery, radiotherapy, chemotherapy, and immunotherapy are part of the therapeutic strategy of oral cancer treatment but also have limitations. Traditional Medicine is an important and proven alternative in the treatment and support of patients with oral cavity cancer. It [is thus desirable to scientifically validate phytochemicals in order to integrate alternative medicine as part of national cancer management strategy. In silico advanced studies on secondary metabolites of medicinal plants traditionally used to treat oral cancer are in p progress.

Key words:

Oral cavity cancer; upper aerodigestive tract; Evidence-based medicine; phytochemicals; medicinal plants; alternative/ traditional medicine.

INTRODUCTION: -

Cancers of the oral cavity (COC) are part of the cancers of the upper aerodigestive tract (UADT) and share the same epidemiological characteristics [1,2]. Cancer of the UADT is the sixth most common clinical form of cancer in the world [3,4,5]. Between 30 and 40% of VADS cancers are oral cavity cancers (OCCs) [6,7]. It often presents as an ulcerated lesion with an indurated base [8,9]. Squamous cell carcinoma is the most common histological subtype and accounts for over 90% of OCCs [6,7,10]. Other types of cancers (salivary gland cancers, sarcomas, lymphomas, melanomas) account for less than 10% of OCCs, and about 1% are metastatic cancers of the lung, breast, prostate, and kidney [11,12]

The development of OCC depends on epigenetic and genetic factors. This tumour process takes place in several stages, starting with some changes in the oral mucosa, followed by the development of invasive cancer until the appearance of

metastases [13]. The aim of this literature review is to discuss the epidemiology of OCC, some risk factors, and means of diagnosis and treatment as well as prevention of OCC. The articles selected for this literature review were in English and French after selection on Google scholar and PubMed search engines from 2010 to 2021. All articles related to OCCs dealing with epidemiology, risk factors, treatment, and prevention were included in this literature review.

Risk factor/ Causes :-

OCC is a multifactorial disease[8], depending on a number of factors that may be unique to the individual and/or related to the environment, genetics, and local and infectious factors. Carcinogenesis takes place in three stages: initiation by which an irreversible lesion is transmitted to so-called initiated daughter cells; promotion during which the initiated cells proliferate and constitute a clone at the origin of the cancer; and finally the progression characterized by local and lymphatic invasion and by metastases. The development of UADT is the consequence of a multi-step process with progressive molecular and genetic changes that ultimately results in the transformation of normal mucosa into invasive cancer. More than 50% of pre-malignant lesions carry a mutation of the P53 tumour suppressor gene. Head and neck cancers express 80–90% of their total epidermal growth factor receptor (EGF-R) repertoire.[8,14,15]

1.Potential malignant lesions:-

Potentially malignant oral epithelial lesions or disorders include both clinical lesions and oral dysplasia, which should be reserved specifically for lesions with histopathological proven foci of dysplasia[16].According to the most recent World Health Organization recommendations[17,18], they have a statistically increased risk of progressing to cancer and are sufficient to cover pre-cancerous lesions and pre-cancerous conditions.

70% of OCCs are preceded by a potentially malignant lesions[6]. Pre-cancerous lesions of the oral cavity mainly include leukoplakia, erythroplakia, submucosal fibrosis, lichen planus, lupus erythematosus, and actinic cheilitis[17,20] . Tobacco and alcohol are the most common risk factors for precancerous lesions of the oral cavity[16,20] . The treatment for these lesions consists of removing the risk factors and monitoring the lesions on a regular basis for early detection of possible transformation into cancer cells [18,19]. However, Ganesh et al. reported that surgery on these lesions does not reduce the rate of transformation of these lesions into oral cancer[21] .

2.Tobacco and alcohol :-

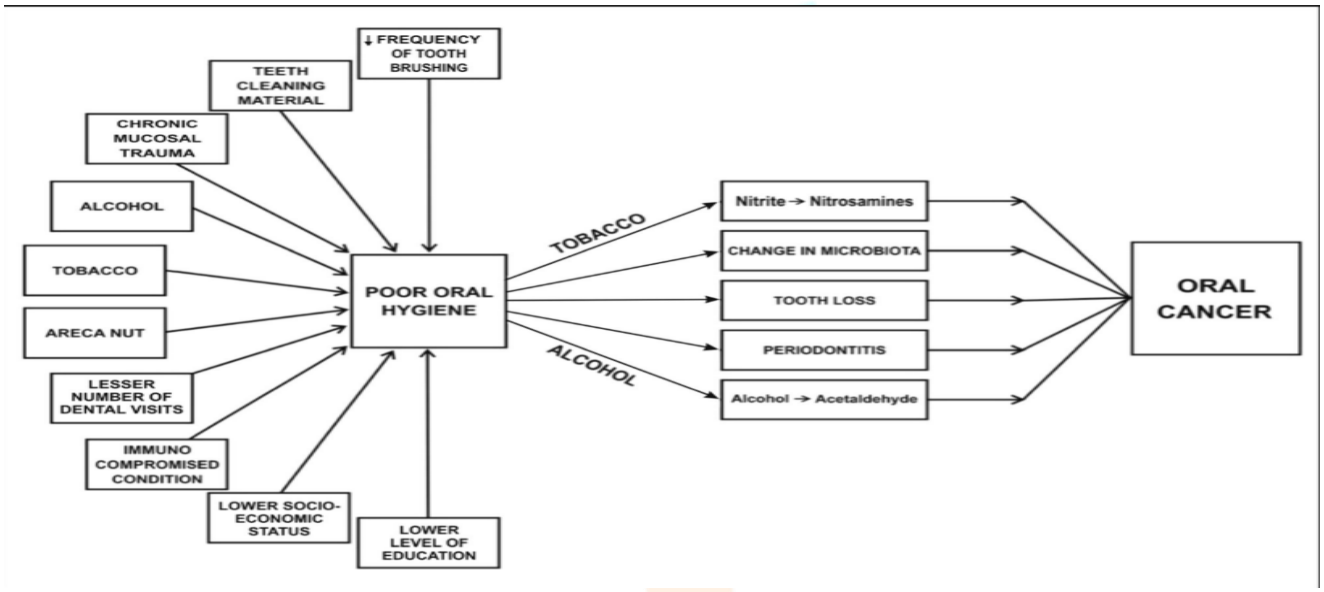
Tobacco use is the leading cause of death in the world, accounting for over 7 million deaths each year, or 44% of all deaths from non-communicable diseases[22] . All forms of tobacco are carcinogenic[23] . 80 to 90% of OCC patients are smokers and the risk increases with the amount of tobacco smoked and its duration[2,24-26] . The use of one pack of tobacco per day for 20 years or two packs per day favors the development of oral cancer [25,27] This can be explained by the fact that tobacco contains several chemical substances, in particular nicotine, which diffuses rapidly into the brain and leads to a strong dependency [2,28]. In addition, tobacco contains polycyclic hydrocarbons and nitrosamines, which are carcinogenic and irritants that interfere with host DNA (desoxyribonucleic acid) and eventually lead to oral cancer [28,31].

Alcohol is classified as a carcinogen by the International Agency for Research on Cancer (IARC) [32]. 75% of people with bluetongue consume alcohol. According to the WHO, more than 3 million people died from alcohol abuse in 2016, i.e., one in twenty deaths worldwide is due to alcohol [33]. Alcohol consumption is a significant risk factor for some chronic non communicable diseases, including cardiovascular disease, diabetes, and certain cancers [33,34]. It is involved in DNA hypomethylation. This leads to loss of control of protooncogene expression, increased mucosal permeability, liver damage, and decreased immunity and salivary flow [13,24,25,27]. Alcohol and tobacco have a synergistic effect on the occurrence of oral cancers [25,29]. Unfortunately, alcohol and tobacco consumption are increasing rapidly in Africa [35].

Oral Hygiene: -

Human herpesviruses (HHVs) and Human papillomaviruses (HPV) are common in the general population and, in immunocompetent people, are mostly carried asymptomatically. However, once an individual becomes immunocompromised by age, illness, or HIV infection these dormant viruses can manifest themselves and produce disease. In HIV-positive patients there is an increased risk of disease caused by HHVs and HPV infections and cancers caused by the oncoviruses EBV, HHV-8, and HPV.

Poor oral health and hygiene are frequently associated with OCC [36,37]. Poor oral hygiene promotes the development of oral cancers by increasing the oral flora with bacteria that will increase the amount of acetaldehyde following the breakdown of ingested alcohol [37,38y through most of the studies found POH as an additive factor in causation of oral cancer [39,40] some studies have reported a stronger correlation between the two [41]. Poor oral hygiene has been hypothesized to contribute to causing oral cancer. However, it may be stated that good oral hygiene may act as a protective barrier against oral cancer.



Factors and mechanisms by which poor oral hygiene can cause oral carcinogenesis

Viruses: -

individual becomes immunocompromised by age, illness, or HIV infection these dormant viruses can manifest themselves and produce disease. In HIV-positive patients there is an increased risk of disease caused by HHVs and HPV infections and cancers caused by the oncoviruses EBV, HHV-8, and HPV. There are over 200 HPV (human papilloma virus) stereotypes, six of which are implicated in cancer, including HPV16 and 18 [42,38] and are more commonly found in normal tissues [38,43]. HPV16 and 18 express the E6 and E7 oncoproteins which inhibit tumor suppressor proteins encoded by the P53 and Rb genes respectively, leading to disruption of cell regulation [4,18,44]. Human herpesviruses (HHVs) and Human papillomaviruses (HPV) are common in the general population and, in immunocompetent people, are mostly carried asymptomatically. However, once an Multiple sexual partners and oral sex with more than six partners may contribute to the development of OCC due to HPV [45]. The carcinogenic role of the HIV (Acquired immunodeficiency syndrome) has also been suggested by a decrease in the immunity of affected individuals, leading to the development of certain HIV-associated tumors in the oral cavity such as lymphomas and Kaposi's sarcoma [45,46]. Epstein-Barr virus (EBV) disrupts host DNA and can result in oral leukoplakia and adenocarcinomas [17,37].

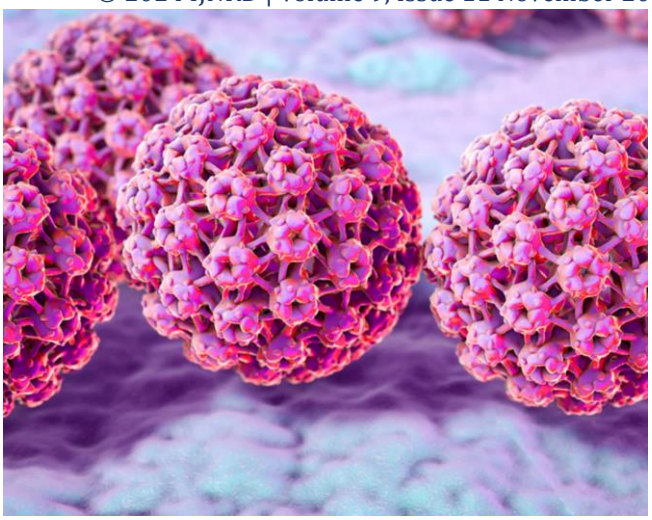


Fig.1 HPV (Human papilloma virus)

Fungal Infections:-

Fungal infections caused by Candida species, in particular, *Candida albicans* has been implicated in the pathogenesis of oral premalignant lesions. Superficial fungal hyphae of *Candida albicans* have been found superimposed on leukoplakia, especially nodular leukoplakia, many of which have undergone malignant transformation. The doubt of whether Candida invasion is a secondary event or causal in oral premalignant lesions is still uncertain and debatable. Candida species are commensals in the oral cavity which become opportunistic during host's immunosuppression due to systemic diseases or drug therapy. Besides immunocompromised individuals, Candida infection can coexist or be associated with other risk factors like irondeficiency and in chronic smokers which may prove synergistic in the development of oral cancer. There is evidence that Candida possesses necessary enzymes fromdietary substances to produce nitrosamines and chemicals that have been implicated in carcinogenesis. A recent study showed relationship between oral yeast carriage and epithelial dysplasia yet again, the actual role of yeast in the development of epithelial dysplasia is uncertain.

Trauma:-

Chronic trauma to the oral mucosa is the repetitive result of mechanical action caused by injury from an irritant [47]. This irritating agent can be a defective tooth (fractured, badly positioned); a bad dental filling [13,47]. Chronic trauma, especially from ill-fitting dentures in the mouth, can be an activator of the carcinogenic process, especially if other risk factors are added [1,15,48]. These chronic microtraumas modify the mucous membrane, leading to keratinization.

IMMUNOSUPPRESSION:-

immunodeficiency virus (HIV)-infected patients are predisposed to developing Kaposi's sarcoma and lymphomas, although not to OSCC. Immunosuppressed organ transplant patients have been shown to develop lip cancers and the possible reason was attributed to increased exposure to solar radiation and other risk factors such as smoking. However, the direct role Immunosuppressed individuals are more prone to develop oral cancers. Human of immunosuppression with lip cancer development was not proven in the studies.

Nutritional factors: -

A diet rich in vegetables and fruit is linked to a reduced risk of oral cancers because fruits and vegetables contain vitamins, particularly A, C, D, and E, which are antioxidants that reduce the risk of cancers of the upper aerodigestive tract [46,49,50]. However, a diet rich in meat, salted and smoked fish increases the risk of developing OCCs due to the presence of nitrosamines, which are carcinogenic [3]

Genetic predispositions: -

Not everyone who is exposed to carcinogenic factors can develop cancer; only a proportion develops it as a result of factors intrinsic to the individual [15,29]. The deleterious effect of a particular carcinogen varies from one person to another and from one region to another [15]. The P53 protein is a tumor suppressor gene thatprevents carcinogenesis by triggering cell cycle arrest, and 40-70% of OCCs have mutations in the P53 gene, leading to the formation of a nonfunctional product [51]. 90% of these mutations are located between exons 5 and 8 of TP53, which is a region where most mutations occur, including R175, G245, R248, R249, R273 and R282 in the DNA binding domain [52,53]. Thus, people with syndromes caused by the mutation of certain genes have an increased risk of developing OCC, as in Fanconi anaemia, where this risk is 100 times higher than in the normal population [54,55].

Gender and age: -

OCCs are more common in men than in women [55,56]. The use of alcohol and tobacco is thought to be at the root of this male predominance of OCCs. Although a female ascendancy has been noted following an increase in tobacco and alcohol consumption in women [15,57], according to a study by Luo et al. [58], the high levels of hormones, particularly oestrogens, in women play a protective role against OCC compared with men. A median age of around 50 has been found in the majority of studies [59,61].

However, due to the increased use of tobacco and alcohol among young people, several cases of cancer have been observed before the age of 50 [62]. HPV infection and genetic predisposition are thought to be the basis of this infection in young people, as well as risky sexual behaviour such as oral sex [62,63].

Exposure to the sun uv rays: -

Exposure to UV (ultraviolet) radiation from the sun is a risk factor for lip cancer. The lower lip is the most exposed to this disease [64,65]. The people most affected by this cancer are outdoor workers such as farmers, fishermen, masons, etc. [65,66]. This lesion often appears between the fifth and seventh decades as a result of accumulated exposure to UV radiation from the sun [65,67].

- Limit sun exposure

  Wear a wide-brimmed hat and use lip balm with a sun protection factor (SPF) of at least 30 to block UVA and UVB rays.

- Follow safe sun practices
  Sun exposure is one of several risk factors for oral cancer, along with tobacco use, excessive alcohol consumption, and HPV infection.

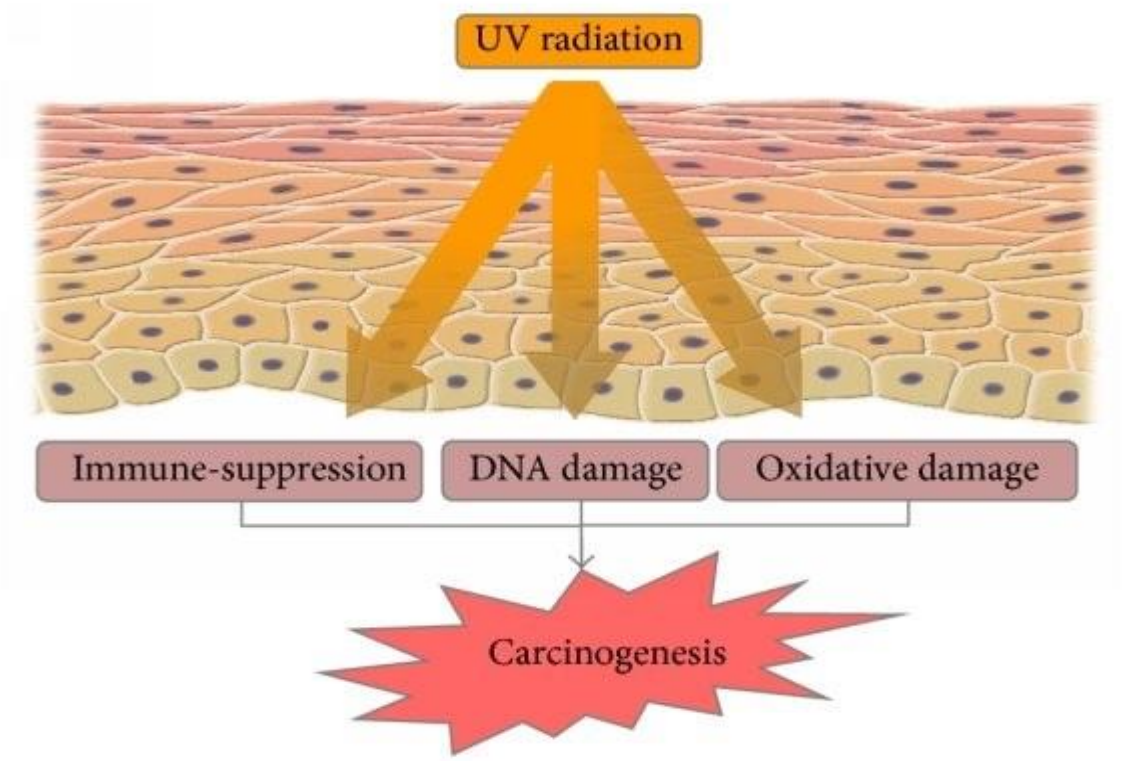


Fig .2 Uv rays effect the skin and cause oral cancer.

3 Other Factors: -

Marijuana use, betel nut addition, people with low social status, mouthwash containing alcohol, chronic candidiasis, and again [13 15,19]. These factors cause the mouth cancer.

Location: -

The tongue is the site most affected by OCC [68,69,70]. This can be explained by the central position of this organ in the oral cavity. It is constantly exposed to carcinogenic substances such as tobacco and alcohol [85, 86] and plays an important role in mastication, phonation, and swallowing [70].

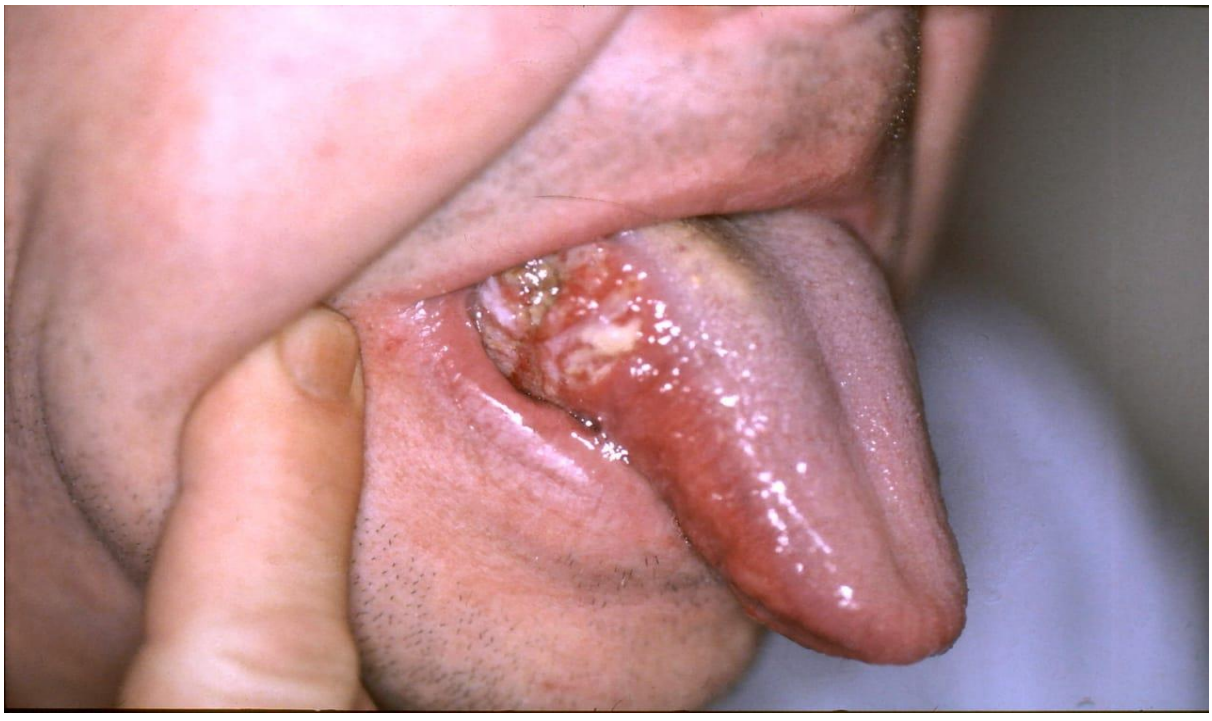


Fig .3 LOCATION OF ORAL CANCER

Cancer of the tongue occurs most frequently in men aged 60-70 years [70,72]. Other common sites of OCC are the lips due to sun exposure and smoking, the gums, the floor of the mouth; and the inner cheeks due to certain habits such as alcohol and chewing tobacco consumption [73,74]

Inflammation and Oral Cancer:-

Inflammation is the main feature of cancer [75]. About 15% of cancers are due to inflammatory processes [76]. Chronic inflammation plays an important role in the development of VADS cancers [75,79]. Several inflammatory mediators are involved in OCC carcinogenesis, including nuclear factor kappa B (NK-KB), vascular endothelial growth factor (VEGF), p53, nitric oxide (NO), reactive oxygen species (ROS), nitrogen species, specific micro RNAs (miRNAs), cytokines [tumor necrosis factor alpha (TNF-α), interleukins (IL-1, IL-6, IL-8)], prostaglandins, and COX-2 (cyclooxygenase 2) [76,82].The expression of these mediators is largely responsible for a pro or anti-tumorigenic inflammatory response through changes in cell proliferation, cell death, cell senescence, DNA mutation, and DNA methylation[76,80]. These inflammatory mediators are involved in angiogenesis, tumor growth, and the proliferation of tumor metastases [76-85]. NO (Nitric oxide) plays an active role in free radical and tumor biology [86].

Overexpression of COX-2 is found in 80% of potentially malignant lesions and cancers of the UADT and this overexpression is associated with lymphatic metastasis [85].

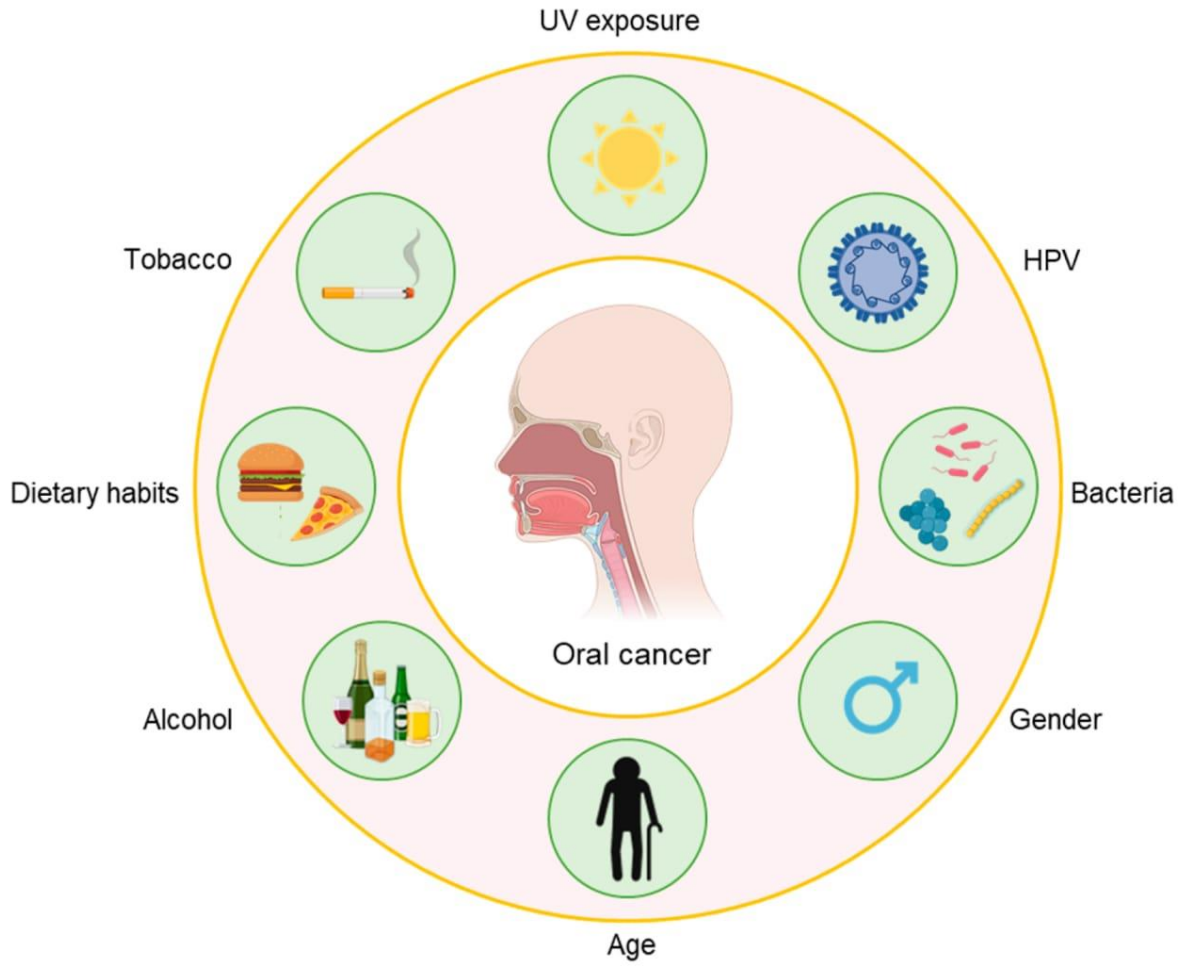


Fig.4 risk factors /causes of oral cancer

Symptoms of oral cancer :-

• Non healing ulcer with or without induration / nonhealing socket • White patch with firm consistency • Red lesion or lesion with erythematous appearance (Erythroplasia) • Abnormal lump in the mouth with increase in size • Exophytic/ulcer proliferative growth • Mass or lump in the neck and neigbouring regions (Lymph node

enlargement) • Mobility/ displacement/ non vital teeth/peri implantitis • Tooth pain and referral pain • Bleeding from the mouth (hemorrhage)

Non-Healing Ulcer: - Ulcerations in the mouth may exhibit from a simple to highly complex variations suggestive of oral malignancy. In other words, patients present with this chief complaint of

"ulceration" depicting to the epithelium and connective tissue damage with the existence of an obvious central crater caused by oedema or proliferation in the surrounding tissue.1 Health care professional must clearly grasp the distinction between malignant/ premalignant lesions from the group of reactive lesions persisting for more than two weeks following the removal of etiological factors. These lesions become more suspicious when it increases in its intensity and turns non responsive to the ongoing treatment.

White Patch with Firm Consistency: -

Lesions appear "white" due to the reflection of the spectrum of light by abnormal keratin and constant bathing of the hyperkeratotic tissue in saliva, analogous to the appearance of palms and soles when immersed in water for long periods.[86] These lesions predominantly are seen in the tongue, floor of the mouth and buccal mucosa. Non-scarpable firm white lesions could be sub categorized as heterogenous or homogenous groups. White papillary lesions of heterogenous variant measuring more than 1 cm usually denotes Verrucous carcinomas. Malignancies associated with these white patches includes Squamous cell carcinoma and Its variants.

Red Patch (Erythroplasia) or Mixed White and Red Patch/ Lesions: -

Red patches differ from early flat lesions to raised blotches or lumps complicating the clinical scenario and prognosis of the patient. These lesions appear true, velvety, red homogeneous to granular, velvety hetereogeneous lesions in nature. They occur most commonly on the lateral surface of the tongue and floor of the mouth indicating the sites of poor prognosis.[87]Areas of redness and inflammation as changes of mucosal abnormality, at high-risk sites persisting for more than 14 days without any obvious etiology or resolution should be biopsied and treated promptly. Unlike leukoplakia or other mixed lesions, persistent asymptomatic or symptomatic erythroplastic lesions at any site should be considered to be invasive carcinoma or at the very least carcinoma in situ. These lesions at high-risk sites also indicate the earliest and predominant sign of oral Squamous cell carcinoma. Common oral malignancies presented as red lesions includes Invasive squamous cell carcinomas,[88] Kaposi sarcoma and Basal cell carcinoma.

Abnormal Lump in the Mouth with Increase in Size:-

Many of the oral malignancies present as an abnormal lump which usually increase progressively in size. The surface would be smooth, erythematous, or ulcerated due to secondary trauma. The site occurrence would include either soft tissues or jaw bones. Common malignancy with this sign includes Squamous cell carcinoma,4 Basal cell carcinoma, Salivary gland malignancies, Sarcoma,[89] Melanoma,[90] Lymphoma, Intra osseous malignancies of maxilla and mandible and Metastatic malignancies.

Exophytic/ Ulcer proliferative Growth: -

Exophytic lesions depicts an uncontrolled pathological growth of the oral mucosal surface with erythematous or mixed appearance. They usually occur in the buccal mucosa, alveolar ridge of maxilla and mandibl of floor of the mouth and the palate. Common malignant lesions with exophytic/ulceroproliferative nature of growth includes, Squamous cell carcinoma and its variants. Verrucous carcinoma account for 4.5-9% of oral squamous-cell carcininomas which typically present as a slowly enlarging, gray or white, warty, exophytic growth on the buccal mucosa or gingiva of elderly men at the time of examination. Other tumors which may appear as exophytic include Sarcomas,[89] Salivary gland neoplasms, Sialadenoma papilliferum with malignant changes, [91] Metastatic tumors and Multiple myeloma.[92]

Oral Cancer Treatment: -

Several treatment protocols for oral cancer exist and depend on the nature of the cancer, the age of the patient, and the TNM (Tumor node metastasis) stage [93-95]. The treatment plan for OCC is decided in a collegial manner in an interdisciplinary meeting after clinical, radiological, and endoscopic assessment . Surgery remains the main treatment for OCC but is associated with massive disfigurement, inability to perform normal oral functions, psychosocial stress, and extensive rehabilitation [10,94-96].

Radiotherapy, chemotherapy, or immunotherapy is also part of the therapeutic armamentarium, and palliative treatment is indicated for nonoperable cases [10,93,96]. Radiotherapy and chemotherapy also have limitations in terms of significant toxicities or resistance to treatment, all of which compromise patients' quality of life and well-being [94,96]. In addition, recurrence and/or metastasis are found in more than half of patients after several years of primary cancer treatment (80% of the cases occur after the first two years), leading to recurrent cancer growth [93,97]

Radiation therapy:-

patients with OCC with an alternative to surgical treatment. EBRT has similar cure rates of patients in early stages, although complications may limit its use in early tongue cancers and other subsites of the oral cavity. Studies have shown a survival benefit for patients receiving accelerated fractionated radiotherapy for HNSCC, although these techniques do not seem to have reached widespread acceptance. Most of the recent evidence using radiation therapy in treating HNSCC surrounds the combined usage of chemotherapy with radiation therapy for patients with advanced HNSCC, although these studies were not evaluating OCC alone.

• Salivation, mucositis, and xerostomia remain important factors in the treatment planning and medical management of patients with complications related to radiation. Studies have revealed a potential benefit from various drugs in patients during and after radiation treatment. In addition, future studies may determine the indications for drugs in combined chemotherapy and radiation therapy

Chemotherapy: -

• Systemic antineoplastic drug therapy (chemotherapy) is not a curative single modality in epithelial HNSCC, but it has an important adjunctive role. Postoperative adjuvant chemotherapy is not the standard of care for HNSCC. There is no benefit from postoperative adjuvant chemotherapy for patients who have undergone surgical resection and are at low risk for recurrence after surgery. Ongoing randomized trials focus on high-risk patients, defined by the Radiation Therapy Oncology Group (positive margins of resection, two or more positive regional lymph nodes, or extracapsular extension), who have undergone surgical resection. chemoradiotherapy is appropriate primary therapy for patients with unresectable OCC, and is being considered as neoadjuvant therapy before definitive surgery. Based on the favourable data from other HNSCC sites, concomitant chemoradiotherapy is superior to radiation therapy alone and should be used for patients able to tolerate the additional toxicity of the combined therapy For patients with recurrent OCC, chemotherapy alone is palliative. Most regimens have used cisplatin with fluorouracil or paclitaxel; hydroxyurea, carboplatin, and docetaxel have also been used in combination with radiation therapy.

TRADITIONAL MEDICINE IN THE TREATMENT OF ORAL CANCER (Evidence based): -

More than 80% of the world's population uses traditional medicine for cultural, economic, or accessibility reasons [98]. Several studies worldwide have confirmed the importance of this medicine in the treatment of cancers in general and those of the oral cavity in particular [99-101]It is currently recognized that modern cancer therapies have demonstrated their limitations in terms of their inability to eliminate tumor cells, drug resistance, and other adverse effects [99-100]. Given these drawbacks, there is a growing interest in traditional medicine, particularly herbal medicine, which is used by 80% of the population in developing countries for the treatment of various diseases, including cancer [99-101]. There is evidence that this medicine improves the effectiveness of

chemotherapy, radiotherapy, targeted therapy, and immunotherapy [100]. It is believed to act on cancer by inhibiting tumor progression and improving the immune system [100]. Medicinal plants have been widely used as a natural source of remedies to cure multiple diseases, including cancer [102]. Among the most widely used herbs are: green tea extract, which contains large amounts of polyphenols including epigallocatechin 3-gallate (EGCG), has anti-cancer and anti-inflammatory properties and induces cell cycle arrest and apoptosis by activating p53 and targeting p21 and Bax [103,104].. Ginger contains gingerol, paradol, and zingerone, and has antioxidant, anti-inflammatory, anti-ulcerogenic, and anticarcinogenic properties [105]. Turmeric is a spice derived from turmeric (Curcuma longa), has anticarcinogenic properties in UADT cancers as a result of its anti-inflammatory effects in decreasing NF-KB and pro-apoptotic regulation Turmeric has a phagocytic action on free. radicals, inhibits lipid peroxidation and decreases tumor cell proliferation by suppressing angionesis and reducing tumour growth and metastasis by activating p53p21[13,105,106]. According to the study by Wang et al. coffee consumption reduces the risk of oral cavity cancer [130]. Garlic, honey, polyphenols, flavoids, anthocyanins, saffron, lycopene, and raspberry also have anti-cancer properties against OCC [13,105,106,108].

. Traditional medicinal plants used in oral cancer treatment: -

. Green tea extract: -

Fig .5 GREEN TEA EXTRACT

Green tea extract belongs to family camellia sinesis plant.

Green tea extract, which contains large amounts of polyphenols including epigallocatechin 3-gallate (EGCG), has anti-cancer and anti-inflammatory properties.

Green tea extract is a concentrated form of green tea that contains antioxidants, flavonoids, vitamins, and other compounds.

Green tea extrct help maintain cell health and prevent cancer.

Ginger :-

Fig. 6 GINGER

Ginger belongs to family gigiberaceae.

Ginger contains gingerol, paradol, and zingerone, and has antioxidant, anti-inflammatory, anti-ulcerogenic, and anticarcinogenic properties [105]

Ginger contains many chemical constituents, including:

- Gingerol: A yellow liquid that gives ginger its characteristic burning taste. Gingerol is considered to be the most therapeutic compound in ginger, with anti-inflammatory, antiviral, antioxidant, and antibacterial properties.
- Shogaol: A volatile oil that contributes to ginger's flavour and odour.
- Paradol: A derivative compound of gingerol and shogaol that has antioxidant and anti-inflammatory properties.
- Zingerone: The active ingredient that gives ginger its pungent hot flavor.
- Zingiberene: An aromatic constituent of ginger.
- Bisabolene: An aromatic constituent of ginger.
- Carbohydrates: Make up 50–70% of ginger rhizomes.
- Lipids: Make up 3–8% of ginger rhizomes. Ginger (Zingiberofficinale Roscoe) is a popular spice particularly in Asia and contains abundant bioactive components that promote the health (Ghasemzadeh et al., 2010). Ginger oil scavenges superoxide and hydroxyl radicals, and inhibits lipid peroxidation in vitro. It considerably decreases the dextran- and carrageenan-induced acute inflammation (Jeena et al., 2013).
-

Turmeric/ curcumin: -

Fig.7 TURMERIC /CURCUMIN

Turmeric (Curcuma longa) is a member of the ginger family, Zingiberaceae.

Turmeric is a spice derived from turmeric (Curcuma longa), has anticarcinogenic properties in UADT cancers as a result of its anti-inflammatory effects in decreasing NF-KB and pro-apoptotic regulation. Turmeric has a phagocytic action on free radicals, inhibits lipid peroxidation and decreases tumor cell proliferation by suppressing angionesis and reducing tumor growth and metastasis by activating p53 and p21 [13,105,106]

GARLIC: -

Fig.8 GARLIC

Garlic belogs to family Amaryllidaceae.

Garlic has a higher concentration of sulfur compounds (allicin, diallyl disulfide, S-allylcysteine, and diallyl trisulfide), which are responsible for its therapeutic properties. It is consumed either raw (fresh leaves or dried cloves) or processed (garlic oil, garlic extracts, and garlic powder), with varying chemical compositions and bioactive ingredient levels. It is long been known as a beneficial spice and a popular treatment for a variety of diseases and physiological conditions.

HONEY:-

Fig .9 HONEY

It belogs to Apidae family.

Current studies show that honey may exert anticancer effects through several mechanisms. Investigations have indicated that honey has anticancer property through its interference with multiple cell-signaling pathways, including inducing apoptosis, antimutagenic, antiproliferative, and anti-inflammatory pathways. Honey modifies the immune responses.

SAFFRON: -

Fig.10 SAFFRON

Saffron belongs to family Iridaceae. It is also known as crocus sativus. The chemical composition of saffron has been studied in detail by various authors. Chemical analysis has shown the presence of more than 150 components in the stigmas of saffron. In addition to the three main components in saffron (crocetin esters, picrocrocin and safranal), it also contains other carotenoids, carbohydrates, raw fiber, proteins, fats, anthocyanins, flavonoids, vitamins (riboflavin and thiamine), minerals and many other elements which confer nutritional properties and are beneficial to health.

Cinnamon: -

Fig .11 Cinnamon

Cinnamon belongs to lauracea family. Cinnamon extract contains several active components such as essential oils and tannin with many biological functions like antioxidation, antimicrobial, anti-inflammatory, anti-diabetes, and anti-tumor activity (Kwon et al., 2010). Kwon et al., (2010) study concluded that the anti-cancer effect of cinnamon extract was directly related to the Figure 2. Comparison of Dual, Triple, and Quadruple Combination of Studied Herbs by Their IC30s in 24 and 48-hour Evaluation. Asian Pacific Journal of Cancer Prevention, Vol 21 483 DOI:10.31557/APJCP.2020.21.2.479 Oral Squamous Cell Carcinoma and Traditional Medicinal Herbs augmentation of apoptosis and inhibition of NFκB and AP1 activity. Yang et al., (2015)

CONCLUSION: -

This review shown the different facets of OCC in terms of both epidemiology and management. OCC is a multifactorial disease involving several endogenous and exogenous risk factors. Knowledge of the epidemiology, the different risk factors, the crucial role of inflammation and genetics in the development of OCC, as well as the different diagnostic and treatment techniques, is necessary for the screening and management of cancer patients. Surgery, radiotherapy, chemotherapy, and immunotherapy are part of the therapeutic strategy of oral cancer treatment but also have limitations. Traditional medicine is an important and proven alternative in the treatment and support of patients with oral cavity cancer. It is thus desirable to scientifically validate phytochemicals in order to integrate alternative medicine as part of the national cancer management strategy. In silico advanced studies on secondary metabolites of medicinal plants traditionally used to treat oral cancer are in progress.

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