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Epidemiology of Oral Cancer

A Project

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By

Anfal Khudier Abood

Supervised By

Dr. Ahlam Taha Mohammed

B.D.S., M.Sc.Ph.D

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Supervision Declaration

This is to certify organization and preparation of this project has been made by the graduate student **Anfal Khudier Abood** my supervision at the Collage of Dentistry, University of Baghdad in a partial fulfillment of the requirement for the degree of B.D.S.

Signature:

Dr. Ahlam Taha Mohammed

B.D.S., M.Sc.ph.D

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1. Introduction

Oral cancer considered as one of the list of head and neck cancer, it is the cancerous growth of tissue located in the oral cavity (Weming, 2007). New oral cancer cases were reported to increase annually over the world for this reason, these disease considered as a major health problem worldwide (Ferlay *et al*., 2008). The oral cancer stand in the range of the sixth most prevalent cancer reported internationally with a yearly incidence of over 300,000 cases, 62% of which exhibit in developing countries (Waranakulasuriya, 2009). The prevalence and incidence of oral cancer worldwide have been widely documented, incidence rate of oral cancer is widely different by geographic location, even within one location, the incidence varies among groups categorized by age, gender or race, and also incidence rate varies over time (Moore *et al*., 2000). These variations in the prevalence of oral cancer indicate that the socio cultural lifestyle of a population plays an important role in the etiology of oral cancer, in addition to the practices of tobacco smoking and drinking alcohol which are established cultural risk factors for oral cancer worldwide (Conway *et al*., 2006). In the other word, variation in pattern and incidence of oral cancer can occur as a result of differences of risk factors, from regional point of view the oral cancer has well defined risk factors that may be modified the focus on the primary prevention which may give a hope to overcome this lethally disease, oral cancers are typically detected in their late stages in spite of the fact that oral cavity can accessible easily for visual examination (Warnakulasuriya, 2009). Oral cancer lesions have well defined clinical diagnostic criteria, hence the early detection of this disease may not improve the cure rate only, but also may help in the decreasing the cost and morbidity rate associated with the treatment of this disease (Sankaranarayanan *et al*., 2005).

2. Oral cancer

2.1 Definition

Oral cancer is the growth of abnormal cells in any part of the mouth or lips most oral cancers start in the lining of the lips or mouth where you have thin, flat cells called squamous cells (Chepeha *et al.*, 2015). It has different levels of differentiation and a propensity for lymph node metastasis although most oral cancers probably arise in clinically normal mucosa some are preceded by a precancerous lesion which indicates an increased risk of cancer development at a particular site, the histopathologist's role is to recognize pathological features which indicate high risk and to provide prognostic information from examination of excised tumors (Barnes, 2005).

2.2 Classification of oral cancer

There are different types of oral cancers, which including the basal cell carcinomas, squamous cell carcinomas, varicose carcinomas, malignant melanoma, mucoepidermoid carcinoma, ameloblastoma , nasopharyngeal carcinomas and so on; but about a high percent of these types are squamous cell carcinomas which originating in the tissues of the mouth and lips high rate of the different types of carcinomas of mouth can at the end become malignant and end results in a squamous cell carcinoma (Khan, 2012). There are different classification system of oral cancer the most common one is WHO classification (2014) Table 1.

Table 1: WHO classification of oral cancer (Asiaf**.,** 2014)

Epithelial cancer	**Salivary gland cancer**
Squamous cell carcinoma	Salivary gland carcinoma
Verrucous carcinoma	Acinic cell carcinoma
Basaloid squamous cell carcinoma	Mucoepidermoid carcinoma
Papillary squamous cell carcinoma	Adenoid cystic carcinoma
Spindle cell carcinoma	Polymorphous low-grade adenocarcinoma
Acantholytic squamous cell carcinoma	Basal cell adenocarcinoma
Adenosquamous carcinoma	Epithelial-myoepithelial carcinoma
Carcinoma cuniculatum	Cystadenocarcinoma
Lymphoepithelial carcinoma	Mucinous adenocarcinoma
	Salivary duct carcinoma
Soft tissue cancer	**Hematolymphoid cancer**
Kaposi sarcoma	Diffuse large B-cell lymphoma
	Follicular lymphoma
	Burkitt lymphoma
	T-cell lymphoma

❖ **Epithelial cancer**

A. **Squamous cell carcinoma (SCC)**

Squamous cell carcinoma (SCC) of Oral Cavity is a common malignant tumor of the mouth considered to be an invasive epithelial neoplasm exhibiting varying degrees of squamous differentiation with a tendency to early extensive lymph node metastases, Figure 1 (Neville *et al*., 2009). Soames and Southam (2010) defined oral squamous cell carcinoma as malignant neoplasm of the oral cavity exhibiting the morphological feature of squamous epithelium and it is the end stage of alteration in the stratified squamous dysplasia when the dysplastic epithelial cell reach the basement membranes and invade the underling connective tissue.

Figure 1: Oral squamous cell carcinoma (Neville *et al.*, 2009).

B. Verrucous carcinoma

Oral verrucous carcinoma (VC), as defined by Ackerman, is a rare, nonmetastasizing, well-differentiated variant of oral squamous cell carcinoma (SCC). Although VC has a slow and continuous local growth pattern; patients with VC have an excellent prognosis, Figure 2 (Rekha *et al*., 2010).

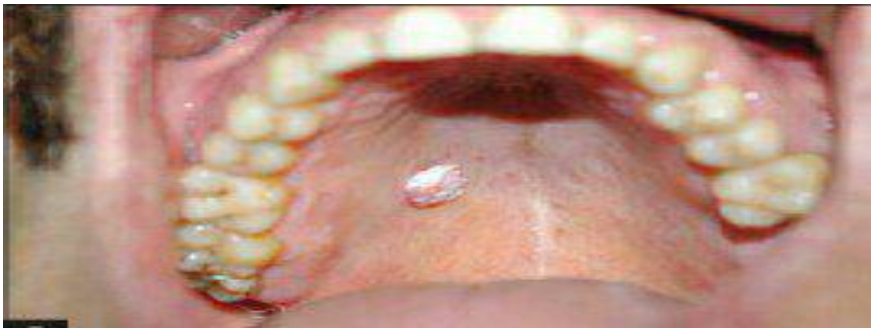

Figure 2: Verrucous carcinoma (Rekha, 2010).

C. Basaloid squamous cell carcinoma

Basaloid squamous cell carcinoma (BSCC) as defined by the World Health Organization is an aggressive, high-grade, variant of squamous cell carcinoma (SCC) composed of both basaloid and squamous components. The tumor arises most frequently in the head and neck region, the most common sites being epiglottis, piriform sinus and base of the tongue, Figure 3 (Fletcher *et al*., 2002; Radhi, 2012).

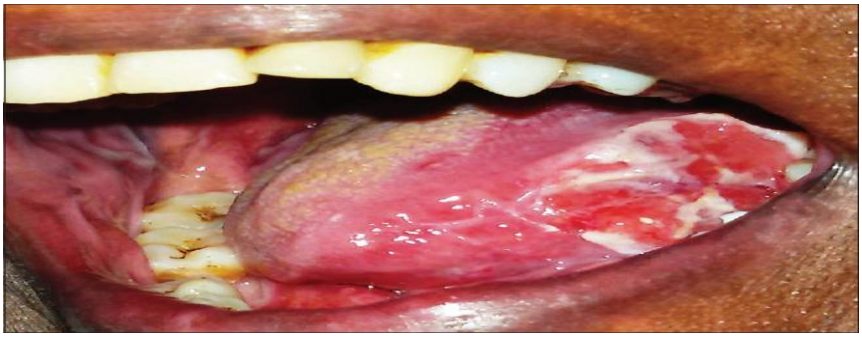

Figure 3: Basaloid squamous cell carcinoma (Radhi, 2012).

D. Papillary squamous cell carcinoma

Papillary squamous cell carcinoma (PSSC) is rare variant of squamous cell carcinoma (SCC). PSCC is characterized by papillary proliferation of SCC cells (Russel *et al*., 2011).

E. Spindle cell carcinoma (sarcomatoid SSC)

Spindle cell carcinoma (SpCC) of the head and neck is a rare, biphasic neoplasm first described by Virchow in 1865 it is composed of squamous cell carcinoma (SCC), either in situ and/or in invasive form, and a malignant spindle cell component with a mesenchymal appearance, but of epithelial origin it accounts for 3% of all SCCs in the head and neck region (Gupta *et al*., 2007).

F. Acantholytic squamous cell carcinoma

Acantholytic squamous cell carcinoma (ASCC) is commonly seen in the sun exposed areas of adults. Their occurrence in the oral cavity is rare and confers bad prognosis Figure 4 (Kerawala, 2009).

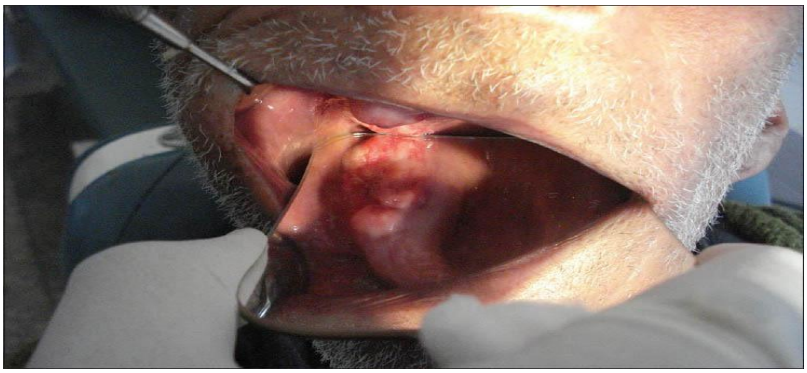

Figure 4: Acantholytic squamous cell carcinoma (Kerawala, 2009).

❖ Salivary gland cancer

Salivary gland tumors usually present as a lump or swelling in the affected gland which may or may not have been present for a long time the lump may be accompanied by symptoms of duct blockage (e.g. xerostomia) usually, in their early stages it is not possible to distinguish a benign tumour from a malignant one one of the key differentiating symptoms of a malignant growth is nerve involvement for example signs of facial nerve damage (e.g facial palsy) are associated with malignant parotid tumours facial pain, classification of salivary gland cancer(2017) seen in Table 2 (Odell *et al*., 2017).

Table 2: Classification of salivary gland cancer (Odell *et al*., 2017)

Benign epithelial tumours	**Malignant Epithelial tumours**	**Hematolymphoid tumours**
Pleomorphic adenoma	Acinic cell carcinoma	Extranodal marginal zone lymphoma of MALT
Warthin's tumor	Secretory carcinoma	
Myoepithelioma	Adenoid cystic carcinoma	
Basal cell adenoma	Polymorphous low-grade adenocarcinoma	
Oncocytoma	Epithelial-myoepithelial carcinoma	
Canalicular adenoma	Clear cell carcinoma	
Lymphadenoma	Basal cell adenocarcinoma	
Sebaceous lymphadenoma	Sebaceous carcinoma	
Nonsebaceous lymphadenoma	Sebaceous adenocarcinoma	
Ductal papilloma	Cystadenocarcinoma	
Inverted ductal papilloma	Low-grade cribriform	
Intraductal papilloma	Cystadenocarcinoma	
Soft tissue lesions	**Borderline tumour**	**Other epithelial lesions**
Hemangioma	Sialoblastoma	Sclerosing polycystic adenosis
Lipoma		Nodular oncocytic hyperplasia
Nodular fascilitis		Intercalated duct hyperplasia

2.3 Risk factors

The major causes of oral cancer worldwide remain tobacco in its many different forms, heavy consumption of alcohol, and, increasingly, infection with certain types of HPV. Although the relative contribution of risk factors varies from population to population, oral cancer is predominantly a disease of poor people (Johnson *et al*., 2011).

2.3.1 Smokeless and smoking tobacco use

Smokeless tobacco in the form of betel quid, oral snuff, and betel quid substitutes (locally called guktha, nass, naswar, khaini, mawa, mishri, and gudakhu) increases the risk of oral precancerous lesions and oral cancer between 2-fold and 15-fold (Javed *et al*., 2010; Gupta *et al*., 2011; Somatunga *et al*., 2012; Gupta., *et al*., 2013).

More than 50 percent of oral cancers in India, Sudan, and the Republic of South Sudan, and about 4 percent of oral cancers in the United States, are attributable to smokeless tobacco products. Smokeless tobacco use among young people is increasing in South Asia, with the marketing of conveniently packaged products made from areca nut and tobacco; as a consequence, oral precancerous conditions in young adults have increased significantly (Gupta *et al*., 2011; Sinha *et al*., 2011).

Consistent evidence from many studies indicates that tobacco smoking in any form increases the risk of oral cancer by two fold to ten fold in men and women International Agency for Research on Cancer (IARC 2004a).The most abundant and strongest being tobacco-specific N-nitrosamines, such as N-nitrosonornicotine and 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (IARC 2007).

The fact that more than 80 percent of oral cancers can be attributed to tobacco and/or alcohol consumption justifies regular oral examinations targeting

tobacco and alcohol users, as well as prevention efforts focusing on tobacco and alcohol control (Radoi *et al.*, 2013).

2.3.2 Areca nut chewing

Areca nut or betel nut, because it is often wrapped in betel leaf, is now regarded as a type 1 carcinogen (IARC, 2007). It is chewed raw, dried, or roasted, or as part of betel quid, by millions of people in Asia; its use is spreading across the Pacific, as well as in emigrant Asian communities worldwide cheap, prepackaged areca nut products, such as pan masala, are of recent concern, especially among youth the inclusion of tobacco in the betel quid adds considerably to the carcinogenicity (Amarasinghe *et al.*, 2010; Johnson *et al*., 2011).

2.3.3 Alcohol use

Epidemiological studies indicate that drinking alcoholic beverages increases the risk of oral cancer two fold to six fold and is an independent risk factor (IARC 2010), with risk increasing with quantity consumed. The risk varies by population and individual and subsite within the oral cavity (Radoi *et al*., 2013). The combined use of alcohol and tobacco has a multiplicative effect on oral cancer risk the various pathways by which alcohol may exert carcinogenic influence include topical exposure leading to a direct effect on cell membranes, altered cell permeability, variation in enzymes that metabolize alcohol, and/or systemic effects, such as nutritional deficiency, immunological deficiency, and disturbed liver function a previous review failed to identify an association between the use of mouthwash containing alcohol and oral cancer risk, or any significant trend in risk with increasing daily use of mouthwash (Gandini *et al*., 2012).

2.3.4 Diet and nutrition

The relationship between diet and nutrition to the risk of cancer development has been established by several epidemiological and laboratory studies (De Stefani *et al., 2000*). The working group of (IARC) has affirmed that low intake of fruits and vegetables predisposes to increased risk of cancer development. More frequent consumption of fruit and vegetables, particularly of carrots, fresh tomatoes, and green peppers were associated with reduced risk of oral and pharyngeal cancer (Dikshit *et al., 2000*). Food and food groups other than fruits and raw vegetables that have a protective effect are fish, vegetable oil, olive oil, bread, cereals, legumes, protein, fat, fresh meat, chicken, liver, shrimp, lobster, and fiber (Jeng *et al*., 2001).

Certain food groups have been shown to be associated with higher risk of oral cancer namely processed meats, cakes and desserts, butter, eggs, soups, red meat, salted meat, cheese, pulses, polenta, pasta or rice, millet, and corn bread (Bernzweig *et al*., 2000).

This has contributed to the significant interest in studies focusing on the macronutrients (proteins, carbohydrates, fat, and cholesterol) and micronutrients (vitamins and their analogs (13-cis retinoic acid and β-D-glucopyranosly ascorbic acid (AA)) and trace elements) present in the food groups that are protective against cancer, Considerable evidence has shown that certain micronutrients decrease the risk of oral cancer development (Negri *et al*., 2000). They include vitamins A (retinol), C (AA), and E (α-tocopherol); carotenoids (β-carotene); potassium; and selenium. β-carotene, retinol, retinoids, vitamin C (AA), and vitamin E (α-tocopherol) are antioxidants that are essential in reducing free radical reactions that can cause DNA mutations, changes in enzymatic activity, and lipid peroxidation of cellular membranes. (Jeng *et al*., 2001).

β-carotene, a major form of provitamin A, are converted to vitamin A in the body (Sankaranarayanan *et al*.,2002). There are over 600 carotenoids in the human body of which only 10% are precursors of vitamin A, although all the mechanisms involved in the anticarcinogenic activity of carotenoids are not known, these agents serve as antioxidants, prooxidants, enhances the immune response, inhibits mutagenesis, reduces the induced nuclear damage (micronuclei), prevents sister chromatid exchanges, protects from various neoplastic events, and protects against photo-induced tissue damage (Jaber *et al.,* 2000).

A direct cause–effect relationship between β-carotene and risk of oral cancer has not been elucidated, this is not feasible as the cancer prevention activity of any substance could be proven only by large-scale randomized, controlled clinical trial lasting for decades (Benner *et al.*, 2000). However, β-carotene supplements have been shown to increase the incidence of lung cancers in smokers (Tolbert *et al*., 2001). Owing to the difficulty in conduction of large-scale prevention trials, considerable interest was shown in the search for intermediate biomarkers which are usually measurable histologic, biochemical, genetic, or other markers that occur during cancer development and which when displayed, places an individual at a higher risk (Stryker *et al.,* 2001). Several treatment trials with β-carotene have been done in oral precancer and cancer and have shown considerable success rates (Zain *et al*., 2000). Remission or regression of oral leukoplakia using β-carotene only or with vitamin A has been shown in many studies. β-carotene is a nontoxic antioxidant to humansand is highly suitable for chemoprevention trials than retinoids such as 13-cis-retinoic acid which exhibit toxicity (Soler *et al*., 2001).

Vitamin C, an antioxidant, decreases nitrosation by preventing the formation of nitrosamines, thereby acting as a chemopreventive agent it also affects the activity of leukocytes and macrophages. AA is also involved in the

activity of cytochrome P450 which is important in the inactivation of potent carcinogens and metabolic activation of procarcinogens (Scully *et al*., 2000). There has been no study reported on the sole use of AA in the treatment of oral leukoplakia. The association between AA and oral cancer is based on the dietary assessments that low intake of fruits and vegetables which are usually rich in vitamin C predisposed to increased risk of oral cancer (Warnakulasuriya, 2012).

2.3.5 Genetic factors

Most carcinogens are metabolized through the cytochrome p450 system in the liver. If this system is defective by virtue of inheriting a particular form of the gene (a polymorphism), the risk of many cancers is enhanced this risk is particularly important with oral and other head and neck cancers, although the relative risks are modest at 1.5 or lower (that is, less than a doubling of risk) (Lu *et al*., 2011).

2.3.6 Sun exposure

Sun exposure increases the risk of developing lip cancer, this is especially true for people who work in the sun for long periods of time, such as farmers, fair skinned people also have a greater risk of developing lip cancer most lip cancers occur on the bottom lip, likely because it’s more exposed to the sun (Johnson, 2016).

2.3.7 Mate drinking

Mate, which is a tea-like beverage consumed in South America and in parts of Europe has been shown to be an independent cause for development of oral and pharyngeal cancers the exact pathogenesis of mate predisposing to oral cancer is still unknown many reasons that have proposed for mate's carcinogenicity are thermal injury, solvent for other chemical carcinogens, and presence of tannins and N-nitroso compounds (Dikshit *et al.*, 2000).

2.3.8 Viral infection

Viruses have been strongly implicated in the development of malignant tumors of the squamous epithelia including the oral squamous epithelium viral infections of latent or chronic nature are usually responsible for inducing malignant transformation by interfering with the host's cell cycle machinery (James *et al*., 2000). These viral genes and gene products may affect cell growth and proliferation. Certain viral genes are proto-oncogenes which become oncogenes when inserted into the host's DNA and ultimately resulting in malignant transformation. The prototypic viruses implicated in oral cancer development are human herpes virus (mainly Epstein–Barr virus (EBV)), human papillomavirus (HPV), and herpes simplex virus (Negri *et al*., 2000).

HPV are the most common viruses implicated in oral carcinogenesis HPV are DNA viruses and are epitheliotropic, especially for squamous epithelia (Karja *et al*., 2008). They cause benign proliferative lesions such as papillomas, condyloma acuminatum, verruca vulgaris, and focal epithelial hyperplasia (Heck's disease) certain HPV types, referred to as 'high-risk' types are associated with OSCC and oral premalignant lesions they are HPVs 16, 18, 31, 33, 35, and 39 the major evidence of the role of HPV in cancer development is that their genes and gene products are capable of disturbing the cell cycle machinery (Cruz *et al.*, 2000). HPV encodes two major oncoproteins namely, E6 and E7. The E6 and E7 proteins have been shown to bind and destroy p53 and Rb tumor suppressor genes, respectively, thereby disrupting the cell cycle with loss of control on DNA replication, DNA repair, and apoptosis HPV has been detected in OSCC, dysplasia, and other benign lesions using various techniques some studies have shown HPV presence in normal oral mucosa making the role of HPV in oral carcinogenesis speculative (Sankaranarayanan *et al*., 2000).

2.3.9 Fungal infection

Fungal infections caused by Candida species, in particular, Candida albicans has been implicated in the pathogenesis of oral premalignant lesions (Zain *et al.,* 2000). Superficial fungal hyphae of Candida albicans have been found superimposed on leukoplakia, especially nodular leukoplakia, many of which have undergone malignant transformation (Swanson *et al.,* 2000). The doubt of whether Candida invasion is a secondary event or causal in oral premalignant lesions is still uncertain and debatabl (Herrero *et al*., 2003). Candida species are commensals in the oral cavity which become opportunistic during host's immunosuppression due to systemic diseases or drug therapy (Copper *et al.,* 2000). Besides immunocompromised individuals, Candida infection can coexist or be associated with other risk factors like iron deficiency and in chronic smokers which may prove synergistic in the development of oral cancer (Hernandez *et al.,* 2003). There is evidence that Candida possesses necessary enzymes from dietary substances to produce nitrosamines and chemicals that have been implicated in carcinogenesis (Stryker *et al*., 2000).

2.3.10 Chronic trauma

It now seems clear that chronic trauma, from sharp teeth, restorations, or dentures, contributes to oral cancer risk, although this higher risk commonly occurs only in the presence of the other local risk factors (Piemonte *et al*., 2010).Generally, oral cancer risk factors could be summarized in Figure 5.

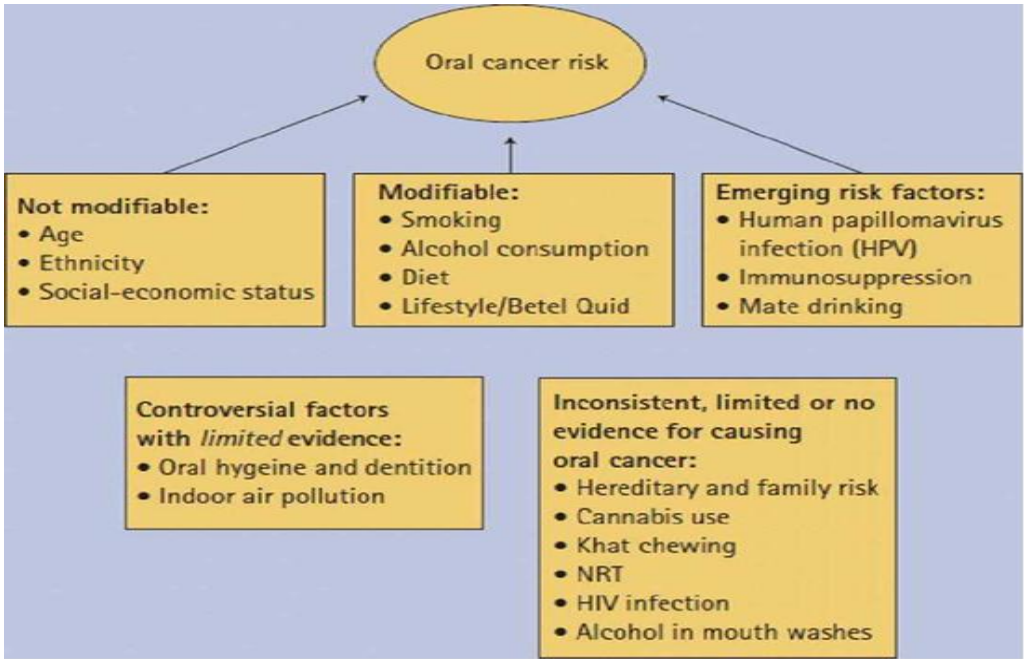

Figure 5: Risk factor of oral cancer (Wamakulasuriya, 2009)

2.4 Epidemiology of oral cancer

2.4.1 Incidence of oral cancer worldwide

Epidemiology of oral cancer is based on the comparison of groups of people for ethical reasons using predominantly observational methods (non-experimental) plays an important role in monitoring and measuring progress in control of cancer (Bland and Daly, 2001). Mouth cancer is a major health problem in many parts of the world, while its incidence is relatively low in most western commoners there are some important exceptions to this trend : on the Indian subcontinent and the other parts of Asia of remains one of the most common forms of cancer and with high rates of incidence data. Significant geographic variation is noted in the incidence of oral cancer noted that the majority of population-based data from the mouth cancer comes from the Western world with a paucity of reliable data the so called developing countries, mouth cancer remains a serious health problem in many parts of the world with many regions reporting increasing incidence rates particularly in males (Moore *et al*., 2000).

In 2011, close to 37,000 Americans are projected to be diagnosed with oral or pharyngeal cancer. 66% of the cases have been found as late stage, only slightly more than half will be alive in five years similar survival estimates are reported from other countries for example, five-year relative survival for oral cavity cancer in Germany is about 55 % (Listl *et al*., 2013).

Iraqi National cancer registry (1976-1994) did not list oral cancer as the most common ten cancers for different periods depending on international coding system for malignancies in this registry, however, cancer of lip, tongue and other sites of the oral cavity are listed as separate entities , thus making each of them out of the range of ten most cancers however, even when considering these regions as part of the oral cavity, oral cancer will not fall within or close to the common tenth cancers in Iraq (Al-Reyahi, 2004).

According to Iraqi Cancer Registry, OSCC accounts for about (4.5%) of all cancer cases in Iraq (AL-Rawi and Al-Talabani, 2007). The incidence of OSCC is about 37/100000 (Taha and Younis, 2015). There are many Iraqi studies showing the percentage of OSCC out of oral cancer (OC), some of these studies are listed in the Table 3.

Table 3: Review of Iraqi studies concerning the percentage of oral squamous cell carcinoma out of oral cancer

Author	Year	City	OSCC percentage out of OC
AL-Reyahi	2004	Baghdad	93.24%
Al- Niamia	2006	Al-Mosul	80.00%
AL-Rawi and AL-talbani	2007	Baghdad	91.50%
Al -Talabani *et al.*	2009	Al-Sulaimania	72.00%
Kuhdier	2012	Al-Sulaimania	56.10%

2.4.2 Age incidence of OSCC

More than 90 % of OSCC are reported in patients over the age of 40 years, after this age there is a sharp and a linear increase in incidence with age (Soames and Southman, 2005). Average age of OSCC, at time of diagnosis, is about 60 years, and more than 95% of OSCC are encountered in patients over 45 years (Chitapanarux *et a*l., 2006). In USA the median age of OSCC at time of diagnosis is 62 years, however, the incidence of OSCC in persons under the age of 45 years is increasing (Wamakulasuriya, 2009).

In the United Arab Emirates (UAE) analysis of the record, the average age of patients with OSCC at time of diagnosis was ranging from 28 to 89 years (Anis and Gaballah, 2013).

Some Iraqi studies demonstrating the relation between incidence of oral squamous cell carcinoma and age group are shown in Table 4.

Table 4: Review of Iraqi studies regarding the oral squamous cell carcinoma by age

Authors	Year	City	Age	Percentage
Al-Reyahi	2004	Baghdad	51-60	28.03%
Al-Reyahi	2004	Baghdad	61-70	28.62%
Al-Rawi and Altalabani	2007	Baghdad	40-70	29.32%
Hassan	2008	Baghdad	40-64	Peak%
AL-Talabani *et al.*	2010	Al-Sulaimaniya	More than 60	78.08%
Al-Kawaz	2010	Baghdad	51-60	Highly affected%
Khudier	2012	Baghdad	50-70	56.10%

2.4.3 Gender incidence of oral squamous cell carcinoma.

According to WHO, carcinoma of the oral cavity in males in developing countries is the sixth commonest cancers after lungs, prostate, colorectal, stomach and bladder cancer, while in females, it is the tenth commonest site of cancer after breast, colorectal, lung, stomach, uterus, cervix, ovary, bladder, and liver (Ravi and Yadav, 2006). Table 5 demonstrates selected literatures that dealt with male to female ratio of OSCC in different countries.

Of all the cancers, oral cancer attributes to 3% in males, opposed to 2% in women new cases of oral cancer in United States as of 2013, approximated almost 66,000 with almost 14000 attributed from tongue cancer, and nearly 12000 from the mouth, and the remainder from the oral cavity and pharynx in the previous year, 1.6% of lip and oral cavity cancers were diagnosed, where the age-standardized incidence rate (ASIR) across all geographic regions of United States of America estimates at 5.2 per 100,000 population it is the 11th most common cancer in USA among males while in Canada and Mexico it is the 12th and 13th most common cancer respectively. The ASIR for lip and oral cavity cancer among men in Canada and Mexico is 4.2 and 3.1 respectively (Neha, 2016).

Table 5: Review of studies regarding Male to Female ratio of oral squamous cell carcinoma.

Author	**Year**	**Country**	**Male: female ratio**
Ajayi *et al.*	2007	Africa	Male>Females
Laronde *et al.*	2008	Canada	2:1
Musavi *et al.*	2009	Iran	6:1
Wamkakulasuiya	2009	India	1.5:1
Shrama *et al.*	2010	India	2.2:1
Sheno *et al.*	2012	USA	4.18:1
Browen *et al.*	2012	UAE	2-4:1

Review of Iraqi studies regarding Male to Female ratio of oral squamous cell carcinoma is presented in Table 6.

Table 6: Review of Iraqi studies regarding Males to Females ratio of oral squamous cell carcinoma.

Author	Year	City	Males: Female ratio
Al-Reyahi	2004	Baghdad	1.35:1
Al-Niamia	2006	Mosul	1.2:1
Al-Rawi and Altalabani	2007	Baghdad	2:1
Hassan	2008	Baghdad	1.2:1

2.5 Prevention of oral cancer

2.5.1 Primary prevention

Primary prevention focuses on avoidance of known etiological factors and alterations in lifestyle to prevent cancer developing in the first place. This is particularly important because oral cancer is one of the few cancers with a high potential for prevention therefore, avoidance of the main etiological and risk factors implicated in the prevention of oral cancer (Mashberg, 2000).

2.5.2 Secondary prevention (CM Marya, 2011)

Focused on inhibition of tumor promotion and progression through:

- Screening of high risk groups.
- Biopsy: any suspicious oral mucosal lesion including any no healing ulcer [more than two weeks] must be biopsied. Biopsy should be sufficiently large to include enough suspect and apparently normal tissues for correct diagnosis. An excisional biopsy should be avoided unless the lesion is very small as it will destroy for the surgeon or radiotherapist the clinical evidence of the site and character of lesion.

- In vitro staining: is advised where it is difficult to decide which is more appropriate area of biopsy, especially if there if there are widespread lesions. Staining with toludine blue followed by a rinse with 1 percent acetic acid and then saline may stain the most suspicious area and indicate those which need to be biopsied.

2.5.3 Tertiary prevention (CM Marya, 2011)

For those who have already been treated for cancer, the prevention of either recurrence or a second malignant tumour is defined here as the third line in prevention through:

- Surgery, radiotherapy, and chemotherapy.
- In order to stop the recurrence and spread of oral cancers, dentists and other health specialists should work together to provide multi-disciplinary support for patients.
- Treated patients may still have dental needs which dentists should monitor to maintain life quality. There may be special needs as well.

2.6 Treatment of oral cancer

2.6.1 Chemotherapy (CT)

In the past, CT was primarily a palliative treatment for oral cancer with the discovery of new drugs, CT has become a significant curative treatment in advanced oral cancer the purpose of CT is to destroy dividing abnormal cancer cells rapidly in order to manage spread and metastasis. CT affects frequently dividing cells, such as those in the oral cavity, skin, bone marrow, alimentary tract, and hair follicles. Current CT techniques have been shown to reduce toxicities, spare sensitive organs such as the spinal cord, optic nerve, and parotid glands, and decrease treatment time while still maintaining quality and accuracy. Overall, CT offers enhanced local control, improved disease-specific survival rates and can contribute to an enhanced quality of life treatment modalities of oral cancer (Haddad *et al.*, 2008; Deng *et al.*, 2011).

2.6.2 Radiotherapy (RT)

There have been significant changes in radiotherapy (RT) in recent years, from new methods of delivery to variation of delivery schedule the changes were made to improve treatment outcomes, preserve tissue, and reduce side effects (Logan, 2009). In general, the intent of RT is to destroy DNA in dividing cancer cells in a localized region while preserving adjacent tissue and function (Haddad *et al*., 2008; Deng *et al*., 2011). RT as a single, primary treatment is not generally used for oral cancer, although it may be used as a sole method of treatment in cases where the location of the tumour makes it difficult to excise, such as the oropharynx, or if the patient refuses surgery (Argiris *et al*., 2008). RT alone has a similar 5-year survival rate to surgery for early-stage disease, with a 37% local recurrence rate in comparison to surgery alone, RT produces milder complications and offers better retention of function and aesthetics, and improved quality of life The use of surgery and postoperative RT is a common combination in oral cancer treatment, used for large tumours and when surgical margins are positive for cancer. RT is usually administered after surgery, as surgery following RT would be hampered by poor healing and an increased risk of infection RT combined with CT is the preferred treatment of oropharyngeal cancers (Schwartz *et al*., 2000; Mazeron *et al.*, 2009).

2.6.3 Surgery

Surgery is the most common treatment for oral cancer (Shah *et al*., 2009). For more advanced tumours, surgery is combined with local radiotherapy (RT) and/or systemic CT (Haddad *et al.*, 2008; Logan, 2009; Deng *et al.*, 2011). The intent of surgery is to completely remove cancerous tissue, leaving histologically normal tumour margins while attempting to preserve normal tissue and function (Sutton *et al.*, 2003; Shah *et al*., 2009).

3. Conclusions

Mortality rates and incidence of oral cancer varies widely throughout the world as the highest amounts have been recorded in India. Oral cancer is serious illness mostly associated with tobacco and alcohol. It should be early diagnosed otherwise sign and symptom will be aggravated .prevention of oral cancer can be achieved through public health promotion in education the people about etiological and risk factors of oral cancer.

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