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Smoking and Oral Cancer: A Statistical Analysis of Patient Cases

Submitted to the College of Dentistry, Al_Mustaqbal University in Partial Fulfillment of the Requirements for the B.D.S. Degree in Dentistry

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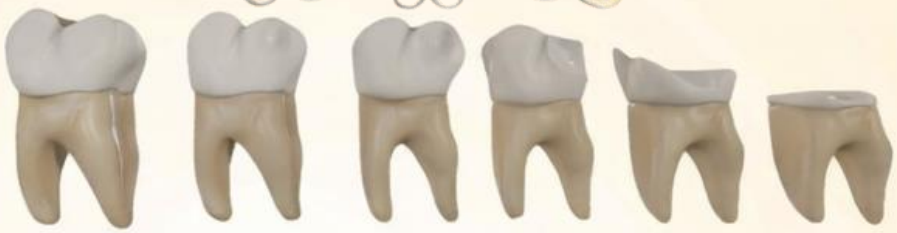
﴿ وَلَا تُلْقُواْ بِأَيْدِيكُمْ إِلَى ٱلتَّهْلُكَةِ ﴾

do not throw [yourselves] with your
[own] hands into destruction

AL QUR'AN/S-BAQARA/195

SUPERVISOR

CERTIFICATE



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Smoking and Oral Cancer:

A Statistical Analysis of Patient Cases

Prepared by (**Ayyat Salem Kadim ،Baneen Abbas Jallab Altamimi ،Ali Hassan Kadim ،Muntadher Thamer Yahya ،Maher Abdul Hussein ،Ali Al-Ridha Najm)** under my supervision at Al-Mustaqbal University, College of dentistry in partial fulfillment of the requirements for the degree of Bachelor in dental and oral surgery (B.D.S)

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DEDICATION

The trip was not short nor should it be

The dream was not close, nor was the path fraught with ease, but I did it and achieved it.

I thank God Almighty first and foremost for the great grace that He has bestowed upon me.

To the one who decorated my name with the most beautiful titles, who supported me without limits and gave me for free, to the one who taught me that the world is a struggle and its weapons are science and knowledge, to the one who instilled in my soul good morals, my first supporter in my path, my strength, and my refuge after God.

To my pride and pride (my father)

To the one whom God made Paradise under her feet, whose heart embraced me before her hand, and made adversity easy for me with her supplications

To the caring heart and the candle that was for me in the dark nights, the secret of my strength and success and the lamp of my path

To the glow of my life (my mother)

To my brothers, sisters, friends and classmates who shared their words of advice and encouragement through all my life.

For everyone who has been a help and support on this path, for our companions over the years and those in adversity and crises

I dedicate to you this achievement and the fruit of my success that I have always wished for. Today, I have completed its first fruit.

I hope that God Almighty will benefit me with what He has taught me.

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First of all, we would like to thank almighty "ALLAH" for inspiring us the energy, patience and strength to accomplish this work.

We would like to express our deep and sincere gratitude to our beloved haet of department (**Dr Athraa Al-Hijazi**) and our research supervisor **Dr. Muayad Hashim Al-Husseini**, for giving us the opportunity to do research and providing invaluable guidance throughout this research. We are extremely grateful to our parents for their love, prayers, caring and sacrifices for educating and preparing us for our future.

ABSTRACT

Oral cancer is one of the most common cancers in the world, making it a major global health concern. More than 90% of cases are oral squamous cell carcinoma (OSCC), which mostly originates from the mouth epithelium. Significant morbidity and mortality are linked to the illness, especially in low- and middle-income nations.

The current study uses statistical analysis of patient data to look at the connection between smoking and the incidence of mouth cancer. Along with alcohol intake, chewing betel quid, viral infections like HPV, poor oral hygiene, and dietary practices, tobacco use—both smoked and smokeless—represents the biggest risk factor.

Early detection has been enhanced by developments in diagnostic methods such as toluidine blue staining, optical imaging, cytology, salivary biomarkers, and artificial intelligence. Improving treatment outcomes and survival rates depends heavily on early .diagnosis

In conclusion, minimizing the worldwide prevalence of oral cancer and enhancing patient prognosis require increasing early detection techniques and limiting tobacco exposure.

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List of Abbreviations

AODS — Antioxidative Defense System
AA — Acetaldehyde
ADH — Alcohol Dehydrogenase
ALDH — Acetaldehyde Dehydrogenase
ASR — Age-Standardized Rate
ATP — Adenosine Triphosphate
BQ — Betel Quid
CYP2E1 — Cytochrome P450 2E1
DNMT — DNA Methyltransferase
DNA — Deoxyribonucleic Acid
DFS — Disease-Free Survival
EBV — Epstein–Barr Virus
ENE — Extranodal Extension
HDI — Human Development Index
HNC — Head and Neck Cancer
HPV — Human Papillomavirus
IARC — International Agency for Research on Cancer
ICD-O — International Classification of Diseases for Oncology
LVI — Lymphovascular Invasion
MENA — Middle East and North Africa
MRI — Magnetic Resonance Imaging
OC — Oral Cancer
OCC — Oral Cavity Cancer
OOP — Oral or Oropharyngeal
OR — Odds Ratio
OS — Overall Survival
OSCC — Oral Squamous Cell Carcinoma
PMD — Potentially Malignant Disorder(s)
PNI — Perineural Invasion
SLT — Smokeless Tobacco
T — Tumor (TNM staging)
TNM — Tumor–Node–Metastasis
WHO — World Health Organization

INTRODUCTION

Head and neck squamous cell carcinoma (HNSCC) represents a significant group of malignancies worldwide, ranking among the most common cancers, with approximately 890,000 new cases and 450,000 deaths annually (Barsouk et al., 2023). These cancers arise in the oral cavity, pharynx, and larynx. Tobacco consumption is considered the most important and well-established risk factor associated with the development of head and neck cancers, in addition to other contributing factors such as viral infections including human papillomavirus (HPV) and Epstein–Barr virus (EBV).

Oral cancer is a general term that refers to neoplasms that originate in oral tissues, it is the 16th most common cancer worldwide, accounting for over 389,485 new cases and 188,230 deaths annually, particularly in low- and middle-income countries (Bray et al., 2024), The prevalence of OCC is relatively high in some Asia-Pacific countries, especially in Taiwan, China, where the incidence rate reaches 32.46 per 100,000 persons (Ferlay et al., 2018), The 5-year survival rate of OCC ranges from 39 to 84% depending on the disease stage and from 48 to 67% for individuals of various ethnicities (Siegel et al., 2020), According to data from the Global Burden of Disease, the overall incidence rate of OC was higher in men than that in women, while women exhibited larger change trends than that demonstrated by men (Du et al., 2020). The primary sites of origin of oral cancers are the lips, anterior two-thirds of the tongue, gums, buccal cavity, and other areas of the oral cavity (Bray et al., 2024).

It is a malignant neoplasm with aggressive behavior; it is considered a worldwide health problem, capable of producing anatomical and physiological sequelae in those who suffer from it and ,eventually, death. It is the most visible and the one that most mutilates the patient from the aesthetic and functional point of view, with difficulties in swallowing, seeing, smelling, and hearing (Montano-Silva et al., 2021). This form of cancer can arise in various regions of the mouth,

manifesting as a painless white lesion that gradually thickens, develops red spots, and eventually evolves into an ulcerative lesion. On the lips, it often appears as a chronic non-healing ulcer that steadily enlarges over time (Marx & Stern, 2023).

The World Health Organization (WHO) introduced a paradigm shift in 2005 by recommending a change in the classification of precancerous lesions to "potentially malignant disorders" (PMDs). This move was motivated by the observation that the majority of oral squamous cell carcinoma (OSCC) cases had evolved from preceding precancerous lesions. The PMDs encompass a spectrum of conditions, including leukoplakia, erythroplakia, oral lichen planus, oral submucosal fibrosis, actinic keratosis, discoid lupus erythematosus, and palatal lesions potentially induced by smoking. These disorders are characterized by their heightened propensity for malignant transformation relative to other oral pathologies (Liu et al, 2016).

More than 90% of malignant tumors in the oral region are squamous cell carcinomas that arise from the mucosal epithelium. However, it's important to identify that these tumors can differ significantly based on their location, etiology, prognosis, and treatment options. (Liu et al., 2016), Oral squamous cell carcinoma (OSCC) typically occurs on the lateral border of the tongue (40%) or the floor of the mouth (30%). It can also affect the lower lip (30%) (Givony, 2020).

Smoking is a major public health issue with profound implications for overall health, including a well-established link to oral cancer, has been strongly associated with tobacco use. The carcinogens present in tobacco smoke, such as benzene, formaldehyde, and nitrosamines, (Umapathy et al., 2024)

Smoking tobacco exposes the mouth and throat to carcinogenic chemicals that can damage the DNA in cells, leading to mutations that cause cancer. Cigarettes contain over 7,000 chemicals, many of which are toxic and at least 70 are known

to cause cancer. The act of inhaling smoke means that these harmful substances come into direct contact with the tissues of the mouth and throat, increasing the risk of developing oral cancer (Umapathy et al., 2024).

Oral cancer is associated with risk factors like chewing betel quid, drinking alcohol, chewing tobacco, and smoking tobacco. Globally, using tobacco with areca nut is the most common risk factor. Prolonged use of tobacco and frequent alcohol intake significantly increase the risk (Singh et al., 2025). Research shows a higher likelihood of oral cancer among those exposed, with varying odds ratios (ORs) in different populations based on product type, cultural practices, and local laws (Nokovitch et al., 2023).

Tobacco is broadly divided into smoked tobacco and smokeless tobacco. Smokeless tobacco is not burnt but is most often snuffed, chewed, or dipped. However, there are more than twenty-eight different varieties of smokeless tobacco being consumed globally12, and in the MENA region it is known through different names such as: shammah ,toombak, maras, nass and neffa. Consumers, who are reportedly adult males (Quadri et al., 2015), place the orally used smokeless tobacco either in their buccal mucosa, labial mucosa or under the tongue, and then suck (dipped) or chew it on a timely basis.

The aim of this study is to perform a statistical analysis of patient cases to investigate the relationship between smoking and the occurrence of oral cancer, providing insights into risk patterns and contributing factors.

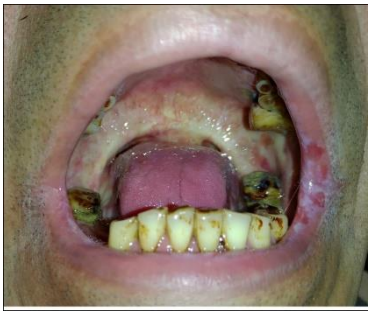

Figure 1. Oral lesions caused by chewing tobacco (Chuang et al., 2022).

LITERATURE REVIEW

Oral cancer ranks among the ten most common cancer locations worldwide, including in Cuba. It is highly visible and causes significant aesthetic and functional disfigurement, severely affecting patients psychologically and influencing their family and social environment. The objective of the original study was to describe the epidemiology of oral cancer. The investigation employed theoretical methods such as analytical-synthetic and historical-logical analysis, in addition to the empirical method of documentary analysis. The behavior of this pathology varies across countries, influenced by lifestyle and living conditions, which are key health determinants. Tobacco use has been identified as the primary risk factor. In Cuba, oral cancer is more frequent among individuals over 60 years of age and predominantly affects males. Despite the existence of an organized program for the early detection of this cancer, and ongoing promotion and prevention efforts, the incidence continues to rise (Abraham-Millán et al., 2023).

Studies show that tobacco smoking is a major risk factor for developing oral cancer. People who smoke are significantly more likely to develop oral cancer compared to non-smokers, and the risk varies between different regions of the world. Smoking habits, frequency, and duration all influence the likelihood of developing the disease (Sadri & Mahjub, 2013).

Tobacco is an important risk factor that can cause epigenetic changes in oral epithelial cells, suppress multiple immune functions, and its toxic metabolites may induce oxidative stress, contributing to oral squamous cell carcinoma. Some viruses, such as EBV and HPV, are also thought to play a role in its development (Jiang et al., 2019).

Smoking and chewing develops a high risk of oral cancer. Most of the tobacco consumers People younger than 30 years used betel-quid in abundance (47.1%).

Bidi was the choice of tobacco for 41-50 age group. In people with less than ten years duration of using tobacco products, gutkha was. consumed in abundance (20.7%). For frequency of 6-10 times per day, smoking Bidi was consumed in 61.4% of instances (Mathur et al., 2009).

Several studies have investigated the association between smokeless tobacco use and oral cancer. Six studies met the selection criteria of a recent review. The included studies examined the effect of shammah, a form of smokeless tobacco. Three case-control studies reported a pooled odds ratio of 38.74 (95% CI: 19.50–76.96), indicating that shammah users had nearly 39 times higher odds of developing oral cancer compared to non-users. The quality of these studies was considered low to moderate according to the Newcastle-Ottawa scale (Quadri, Tadakamadla & John, 2019).

SLT use was strongly associated with oral cancer (adjusted OR: 8.78; 95% CI: 5.14-15.00). Risk was higher in women (OR: 14.33, 95% CI: 6.33-32.42) than in men (OR: 5.29, 95% CI: 2.62-10.67). Male dual users of SLT and smoked tobacco had the greatest risk (OR: 17.23, 95% CI: 5.70-52.01). Analysis by SLT type indicated significant independent associations with oral cancer for both Betel Quid (BQ) usage with tobacco (OR: 8.93, 95% CI: 5.23-15.27) and without tobacco (OR: 4.43, 95% CI: 1.94-10.10). A dose-response relationship was observed, particularly in women. SLT use accounted for an estimated 41% of male and 76% of female oral cancer cases in Bangladesh (Ullah et al., 2025).

Additionally, Males (78.35%) more commonly reported OSCC than females (21.62%), and the majority of them were in the age category of fifth to seventh decades of life. The most affected region was the buccal mucosa with 33.3%, followed by the lower alveolus with 30.63%. The duration of harmful habits varied from one year to more than 40 years, and the majority of the patients had T4a staging (40.54%), followed by T2 staging (29.73%) with a habit duration of more than five years. Approximately 22.52% and 0.9% had PNI and LVI,

respectively. The correlation between the two variables was evaluated using the Pearson correlation test and was found to be statistically significant ($p<0.05$), le., habit to gender and staging with gender were p-0.027 and p-0.028, respectively (Reichal & Prethipa, 2024).

This study highlights that demographic factors, adverse habits, and socioeconomic status significantly influence OSCC risk and severity in Indian patients. The findings underscore the critical need for early detection initiatives, particularly in lower socioeconomic groups, and suggest that reducing tobacco and alcohol use can mitigate OSCC risk. Equipping the primary care physicians with the knowledge of primary prevention and enhanced public awareness to reduce presentation delays and unprove patient outcomes (Sil et al., 2025).

In a large retrospective cohort study, tobacco smoking—evaluated as smoking status and accumulated tobacco exposure (ATE)—was significantly associated with inferior overall survival (OS) and disease-free survival (DFS) among patients diagnosed with oral squamous cell carcinoma (OSCC). Patients who continued smoking after diagnosis had a worse long-term prognosis compared to those who ceased smoking at diagnosis, and the impact of tobacco exposure on survival varied based on tumor subsite and alcohol consumption Andersen et al. (2022).

This study confirms second primary malignancies as a key prognostic factor for survival in OSCC. Male sex, advanced TNM stage, gross ENE, multiple lymph node involvement, and active smoking status were linked to poorer outcomes. Larger studies with multivariate analysis comparing primary and non-primary tumors are needed to validate these findings (Ramirez-Guanche et al., 2025).

Despite extensive evidence linking tobacco use to OSCC development and prognosis, limited data are available regarding patients' behavioral changes

following diagnosis and the effectiveness of cessation interventions, particularly in specific populations

Finally, among patients who were smoking at the time of the OOP cancer diagnosis, 47.7% continued to smoke after the diagnosis. OOP cancer diagnosis was influential in smoking cessation in ever-smoker patients and their cohabiting smokers. The apparent influence of OOP cancer diagnosis was different between cohabiting smokers of ever-smoker patients (n=21/25; 84%) and those of never - smokers (n=10/21; 47.6%). Former-smokers (n=16/19; 84.2%) were less likely to remember receiving smoking-cessation advice than current-smokers (n=17/3943.6 ;% .(Pressure from family and friends, adverse impact on cancer prognosis, and adverse impact of cancer treatment were influential factors for smoking cessation .Among treatment modalities, combined chemoradiotherapy had the greatest impact (n=10/21; 47.6%) on smoking cessation among patients who stated that oncology treatment was influential in causing them to quit or decrease smoking (Gray et al., 2019).

EPIDEMIOLOGY

Because oral cancers fall under the category of head and neck cancers (HNC), a significant amount of research is devoted not only to oral cancer but also to cancers of the tonsils, nasopharynx, oropharynx, salivary glands, and other organs. This makes it challenging to organize data on the epidemiology of oral cancers. As a result, the data in the review that follows is compiled from publications that look at the epidemiology of head and neck and oral cancers.

The 16th most common type of cancer worldwide is lip and oral cavity cancer (Bray et al., 2024). By 2030, the incidence of HNC is predicted to have increased by 30% (Johnson et al., 2020). Global trends in the incidence rate of lip and oral cavity cancer are depicted in Figure 2, which was produced by the GLOBOCAN

website (Bray et al., 2024). Melanesia (ASR 19.8) had the highest incidence, followed by South-Central Asia (13.5), Central and Eastern Europe (10.3), Western Europe (10.0), and Australia and New Zealand (10.0). The incidence of oral cavity, pharyngeal, and lip cancer increases with age, peaking in the 70–85+ age range. Improved early cancer detection and increased exposure to risk factors may be the cause of the rising number of cases in European countries, especially in developed nations. Because rapid socioeconomic growth encourages the adoption of unhealthy lifestyles, behaviors, and environmental factors, it has been noted that countries with low and medium Human Development Indexes (HDI) typically have higher cancer incidence and mortality rates. According to an analysis of substance use across different regions, tobacco smoking and alcohol consumption are major risk factors for oral cavity cancer in Europe. The common practice of chewing betel quid may be a factor in the high incidence of this cancer in Melanesia, South-Central Asia, and South-Eastern Asia. In the meantime, sun exposure has been found to be the most important risk factor linked to the region in some parts of Oceania, especially Australia and New Zealand (Huang et al., 2023), Oropharyngeal cancers associated with HPV infections have been identified as a major contributor to the higher incidence of head and neck cancer in the USA and Europe (Mehanna et al., 2013). It is interesting to see how incidence varies in highly developed nations. Between 2005 and 2010, the incidence of oral cancer in men decreased in France (-12.6%), Spain (-10.8%), and Hong Kong (-10.5%), while it increased in the United Kingdom (+18.8%), Japan (+21.3%), and Australia (+8.7%) (Bosetti et al., 2020). Numerous factors, such as differences in health policies, changes in lifestyle, and other socio-economic influences, can be responsible for the varying incidences of oral cancer observed in different countries. Understanding the causes of the disparate patterns in the incidence of oral cancer in various nations requires taking into account a number of factors, such as the availability and caliber of healthcare, lifestyle choices (such as smoking or drinking), and the nation's current social and

economic circumstances. These factors may have an impact on the incidence and detection of oral cancer, leading to different trends in incidence.

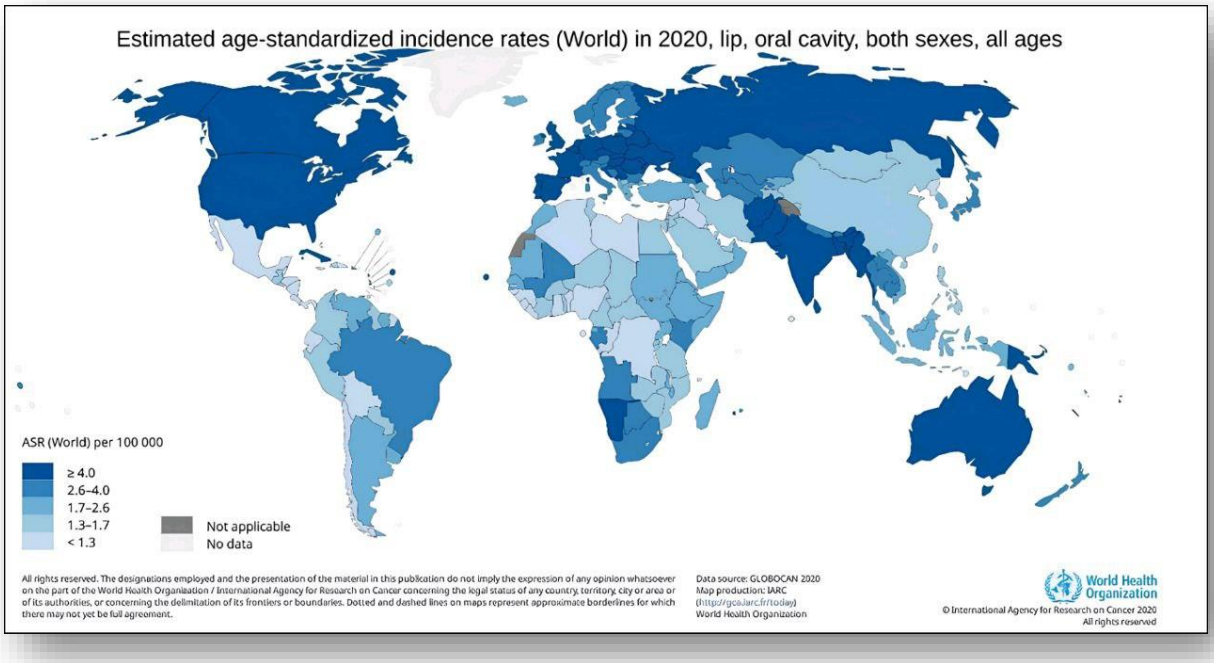

Figure 2. Global age-standardized incidence rates of lip and oral cavity cancer (Bray et al., 2024).

RISK FACTORS: TOBACCO

Smoked Tobacco

Tobacco smoke Oral cavity cancer (OC) has been closely linked to tobacco use, including cigars, pipes, and cigarettes. All oral sites have a higher risk of OC, (Timbang et al., 2019) but the floor of the mouth has the highest risk. According to studies, the risk of developing OC increases with the early onset of tobacco uses as well as the length and frequency of smoking. Due to their higher alkalinity and carcinogenic content, traditional tobacco products like bidis, chutta, and cheroot have been associated with twice the risk of OC in India when compared to industrial tobacco, another risk factor that significantly affects the development of oral cancer is tobacco use. Oral cancer is seven to ten times more common in smokers than in nonsmokers (Zhang et al., 2019). Cigarette smoking is still the

most prevalent addiction, despite a sufficiently high understanding of the hazards (WHO, 2023). Nicotine and carcinogens are two components of cigarettes that, when combined, raise the risk of mouth cancer (Hecht, 2003). Although the IARC does not classify nicotine as a carcinogen, people nonetheless go for cigarettes because of their high potential for addiction, which exposes them to over 60 other carcinogens (IARC, 2023; Hecht, 2003). The fact that fewer people are smoking is promising, and according to WHO, Tobacco users will make up 20.9% of the world's population in 2025, which is 1.9% fewer than in 2020 (22.8%) (WHO, 2023). However, many people—mostly young people—have begun to utilize alternatives like electronic cigarettes. For example, Cole et al.'s study (Cole et al., 2021) in Canada found that the prevalence of e-cigarette use rose from 7.6% (2013–2014) to 25.7% (2018–2019). Research indicates that e-cigarettes are less harmful than traditional cigarettes (McNeill et al., 2019; Javed et al., 2017), however there is now mounting evidence of a detrimental effect on human health because of things like high metal vapor levels (Goniewicz et al., 2014; Williams et al., 2013). Although e-liquids include chemical substances that are cytotoxic to the oral mucosa and other sections of the upper respiratory tract and can be harmful to DNA (Welz et al., 2016), there is currently no compelling evidence that e-cigarettes directly raise the risk of mouth cancer (Tzortzi et al., 2020). Consequently, it is impossible to exclude electronic cigarettes from the category of mutagenic agents.

Smokeless Tobacco

Tobacco without smoke Another important risk factor for OC is smokeless tobacco, which comes into contact with the mucous membranes inside the oral cavity. Oral snuff (wet or moist), chewing betel quid, and other culturally specific products are common forms, especially in Asia, the Middle East, and parts of Europe and North America. Frequent smokeless tobacco use is primarily linked

to verrucous carcinoma, also known as "snuff-dipper's cancer," and oral precancerous lesions. Duration, frequency, and early onset of use all raise the risk.

Alcohol

Alcohol One of the most significant risk factors for oral cancer is alcohol, particularly when combined with tobacco (Bray et al., 2024). It causes cancer of the larynx, pharynx, esophagus, breast, liver, and colorectum in addition to oral cancer. Acetaldehyde, the initial byproduct of ethanol metabolism, is the most mutagenic component of alcohol. Ethanol is converted to acetaldehyde (AA) by cytochrome P4502E1 (CYP2E1) and alcohol dehydrogenase (ADH). Acetaldehyde dehydrogenase (ALDH) further breaks down acetaldehyde into toxic acetate. AA damages the antioxidative defense system (AODS) and results in DNA adducts, DNA repair inhibition, and DNA methylation. Furthermore, reactive oxygen species (ROS) are produced when CYP2E1 oxidizes ethanol which the compromised antioxidative defense system (AODS) is unable to adequately counteract, resulting in the creation of DNA adducts. Additionally, CYP2E1 transforms a number of procarcinogens into their final carcinogenic forms (Seitz & Stickel, 2010). Although ethanol metabolism mostly takes place in the liver, it can also start in the mouth, which could lead to the buildup of a mutagenic concentration of acetaldehyde in saliva. This occurs because the oral cavity's normal microbiome contains bacteria and yeast, which are primarily responsible for the local production of acetaldehyde from alcoholic beverages. Furthermore, elevated ACH levels persist as long as ethanol remains in the human body (Nieminen & Salaspuro, 2018) The estimated range of ACH's mutagenic levels is 40–100 μM. Drinking diluted vodka within 20 to 40 minutes can accomplish this (Seitz & Stickel, 2010). Despite scientific evidence of alcohol's carcinogenic effects, few people are aware of this issue. The percentage of people from various geographic locations who are aware that drinking alcohol increases the risk of oral cancer is displayed in Figure 3. The results of the survey showed

that awareness of alcohol as a risk factor for oral cancer varies significantly between nations. India had the highest level of awareness (64%), followed by Yemen (58.9%) (Al-Maweri et al., 2015) and Italy (58.01%) (Nocini et al., 2020), where over 50% of participants identified alcohol as a risk factor. The United States of America (38%) (Wiseman & Klein, 2019) and Germany (Hertrampf et al., 2012) both had moderate levels of awareness, with 43% of respondents identifying alcohol as a risk factor, whereas the Australian state of Far North Queensland (Formosa et al., 2015) had a lower level of awareness at 33%. Only a small percentage of people in Sri Lanka (17%) and Denmark (15.4%) (Thomsen et al., 2020) are aware that alcohol is a risk factor for oral cancer.

HPV

More than 200 known viruses are collectively referred to as HPV, or human papillomavirus (WHO, 2023). While most infection symptoms are mild, some high-risk HPV strains can cause cancer or genital warts (WHO, 2023). In 2018, 2.1% of newly diagnosed cases of oral cavity cancers were linked to an HPV infection (de Martel et al., 2020). The majority of cases that were found were specifically linked to HPV16 and HPV18 infection (Ndiaye et al., 2014; de Martel et al., 2017). Moreover, HPV16 is the most persistent type, resulting in a longer exposure period (22 months for men and 19 months for women) (Rautava et al., 2012). This directly raises the possibility that the virus will cause cancer in human cells (Beachler et al., 2015). HPV16 and HPV18, high-risk types are regarded as one of the main risk factors for oropharyngeal cancers, but it is still unknown how specifically HPV contributes to the development of oral cancer (Kijowska et al., 2024). The most prevalent type of oral cancer, oral squamous cell carcinoma (OSCC), is strongly linked to HPV, according to some reviews on the subject (Kaur et al., 2024).

DIET

Eating certain foods, particularly those high in pro-inflammatory factors, is also linked to an increased risk of oral cancer. Prolonged inflammation is caused by a pro-inflammatory diet. inflammation, which may encourage the development of cancer in the oral cavity as well as other parts of the body (Hua et al., 2020). Cytokines and other inflammatory biomarkers that play a role in the development and spread of cancer are elevated in diets with high DII (dietary inflammatory index) (Rodriguez-Molinero et al., 2021). Thus, products that may contribute to the development of cancer include, for example, red and processed meat, refined grains, simple sugars, eggs, and high-fat dairy (Malesza et al., 2021; Chang et al., 2017). Eating spicy food or drinking extremely hot tea has been shown to raise the risk of oral cancer on the other hand, there is a group of foods that may prevent oncogenesis. These include citrus fruits, yellow fruits and vegetables , blackberries, cranberries, products rich in omega 6 and 3 acids, garlic, curcumin, and many more (Gupta et al., 2017; Esquivel-Chirino et al., 2023; Mukherjee & Krishnan, 2023).

Oral Hygiene

Bacteria are a major component of pathological plaque, which builds up as a result of poor oral hygiene (Gaonkar et al., 2018). The metabolism of carcinogens (e.g., Streptococcus and Neisseria); (2) the production of carcinogens (e.g., candida produces nitrosamines); (3) the induction of chronic inflammation (e.g., bacteria that cause periodontal disease, Prevotella intermedia, etc.), where the cytokines produced promote cell proliferation and inhibit cell apoptosis; (4) the direct influence of bacteria on cell cycle signals; and (5) bacteria directly damage DNA through toxins.

PATHOLOGY

Link between smoking and oral cancer

Smoking and oral cancer are related Tobacco use exposes the mouth and throat to carcinogenic substances that can harm cell DNA and result in cancer-causing mutations. At least 70 of the more than 7,000 chemicals found in cigarettes are known to cause cancer, and many of them are toxic. Inhaling smoke increases the risk of oral cancer because these toxic substances come into direct contact with the tissues of the mouth and throat (Umapathy et al., 2024) Oral cancer is much more common in smokers than in nonsmokers, according to studies. Oral cancer is six times more common in smokers than in non-smokers, according to the American Cancer Society, the risk rises with daily cigarette consumption and lifetime smoking duration. Those who smoke more than 40 cigarettes a day are considered heavy smokers and are most at risk. (Lisko et al., 2014).

How smoking contributes to oral cancer?

Smoking causes oral cancer through a complicated and multidimensional process. The following are some of the main ways that smoking causes this illness to develop (Natarajan et al., 2024):

1. Direct Exposure to Carcinogens: The cells in the mouth and throat are directly harmed by the carcinogens in tobacco smoke. These cells' DNA undergoes mutations as a result of repeated exposure, which may ultimately result in the development of cancerous tumors.

2. Weakened Immune System: Smoking impairs immunity, making it more difficult for the body to fight off illnesses like cancer and infections. Additionally, a compromised immune system makes it harder for the body to fix damaged DNA, which raises the possibility of cancerous cell alterations.

3. Inflammation and Cell Damage: Smoking results in persistent inflammation in the oral and throat tissues, which breaks down healthy cells and encourages the

development of cancer. Smoking's ongoing irritation can lead to cells proliferating quickly in an effort to repair the damage, raising the risk of mutations and the emergence of cancer. (Azad et al., 2016).

4. Synergistic Effect with Alcohol: People who smoke and drink alcohol are even more likely to develop oral cancer. As a solvent, alcohol increases the absorption of carcinogens in tobacco smoke into the oral and throat tissues. The risk of oral cancer is significantly increased by this synergistic effect.

Effect of Smoking on DNA Methylation and Gene Function

Cigarette smoking is a strong environmental factor that alters DNA methylation, an epigenetic process that regulates gene expression without changing the DNA sequence. Smoking affects both global DNA methylation and gene-specific methylation, leading to changes in how genes involved in cell growth and repair function. These methylation changes are linked to smoking intensity and duration, and they contribute to the development and progression of diseases such as cancer. In addition, the distinct methylation patterns induced by smoking can help distinguish current smokers from former smokers and non-smokers and may be used as biomarkers to predict disease risk (Fragou et al., 2019).

Impact of smoking cessation on oral cancer risk

The good news is that the risk of oral cancer can be considerably decreased by giving up smoking. When a person quits smoking, their body starts to heal and their chance of developing cancer gradually declines. Compared to a current smoker, the risk of developing oral cancer is halved within five years of quitting. The risk is comparable to that of a nonsmoker after ten to fifteen years. Quitting smoking enhances oral health in general and reduces the risk of oral cancer. Gum disease, tooth loss, and other oral health issues are less common in ex-smokers. If they are diagnosed with oral cancer, they also have better results because nonsmokers typically react better to treatment (Natarajan et al., 2024) Quitting smoking is essential for lowering the risk of oral cancer, a condition strongly

associated with tobacco product use. Smoking damages the cells lining the mouth by introducing carcinogenic chemicals into the body, which can cause mutations that result in cancerous growths. Because quitting smoking enables the body to start repairing the damage caused by tobacco, it dramatically reduces the risk of developing oral cancer. Over time, quitting smoking can significantly reduce a person's risk, even if they have smoked for a long time. Additionally, giving up smoking improves the quality of life and overall survival rates for people who have already been diagnosed with oral cancer. Therefore, quitting smoking is an important preventive strategy and a crucial part of oral cancer management and recovery (Kalkhoran et al., 2018).

CLINICAL FEATURES

Oral cancer may arise in any oral cavity subsite (Table 1). According to the affected subsite, clinical features may vary. OC may be detected at its early stages where lesions may appear as asymptomatic small ulcers or lumps. The size of initial OC lesions can range from a few millimeters to several centimeters as the lesions progress. Lesions may appear as erythroleukoplakias with central ulcerations indicating suspicion for carcinoma in situ or invasive squamous cell carcinoma at the time of detection (Figure 3). Late-stage disease however appears as large growths with rolled margins and surface ulcerations (Figure 4). The tongue is a common oral cavity subsite for the development of OC (Figure 5). Suspicious tongue lesions may present as a small growth-like lesion (Figure 6) to a larger ulcerative lesion extending to the ventral surface (Figure 7). Some tumours present within large non-homogenous leukoplakias (Figure 8,9,10). In advanced cases, tumours present as ulceroproliferative growths with areas of necrosis and extension to surrounding structures such as muscle, bone, and layers of the skin with neck metastasis (Figure 11). The floor of mouth represents the second most common site for the development of OC (Figure 12). Lesions are

likely to arise from a pre-existing leukoplakia or erythroplakia (Figure 13). The palate may also be affected with OC when lesions present as non-healing indurated ulcers with a depressed alveolar mucosa (Figure 14). It is worth noting that appropriate retraction of oral tissues aids in the detection of suspicious lumps presenting in edentulous spaces such as the lower posterior alveolar ridge (Figure 15).

Table 1. Anatomical subsites derived from the International Classification of Diseases for Oncology

Lip	Mucosa of upper lip Mucosa of lower lip Commissure of lip Overlapping lesion of lip
Tongue	Dorsal surface of tongue Border of tongue Ventral surface of tongue Anterior two thirds of tongue Lingual tonsil Overlapping lesion of tongue
Gum	Upper gum Lower gum
Floor of mouth	Anterior floor of mouth Lateral floor of mouth Overlapping lesion of floor of mouth
Palate	Hard palate Soft palate Uvula Overlapping lesion of palate
Other and Unspecified parts of the mouth	Cheek mucosa Vestibule of mouth Retromolar area
Salivary glands	Parotid gland Submandibular gland

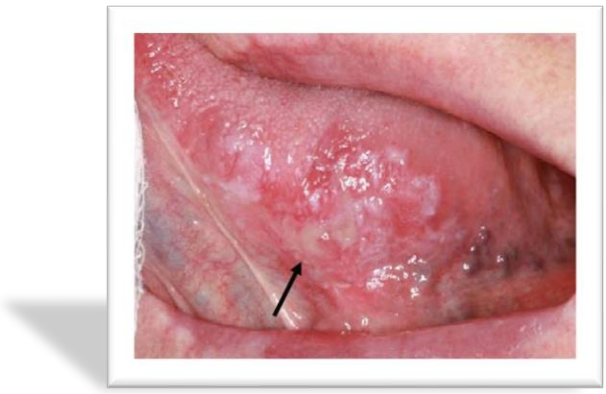

Figure 3 (Tongue) A large erythroleskophia with central alceration Сатов) расонs for OSCC.

Figure 4. (Tongue) An extensive growth-like lesion highly suspicious for OSCC

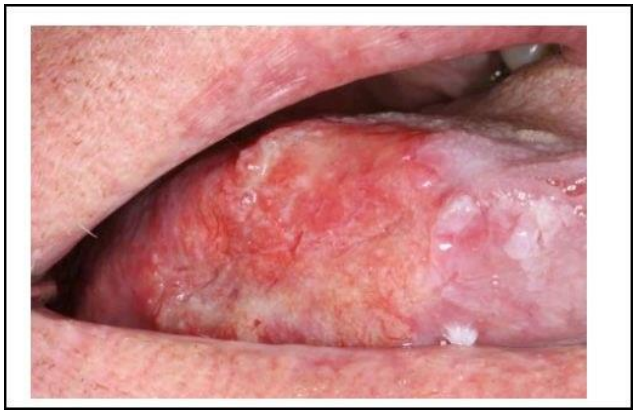

Figure 7. (Tongue) Large ulcerative lesion extending from the lateral to ventral surface of tongue

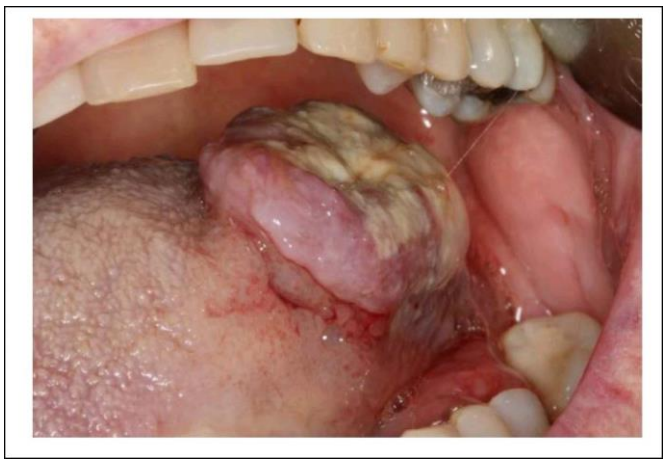

Figure 5. (Tongue) A large growth-like lesion with surface ulceration suspicious for OSCC

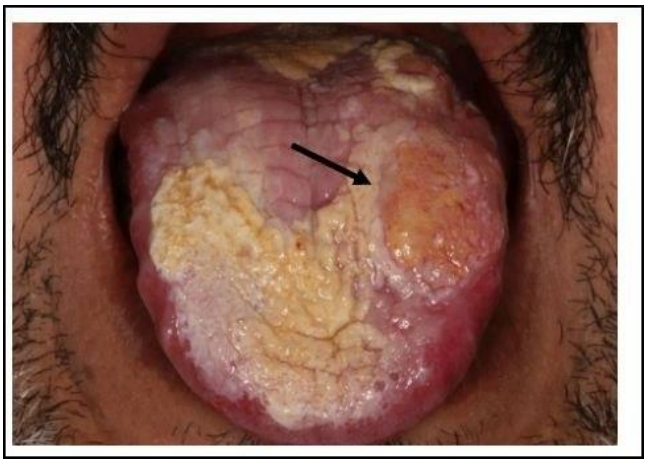

Figure 8. (Tongue) Suspicious tumour in the left aspect (arrow) of the dorsum surface surrounded by an extensive verrucous leukoplakia

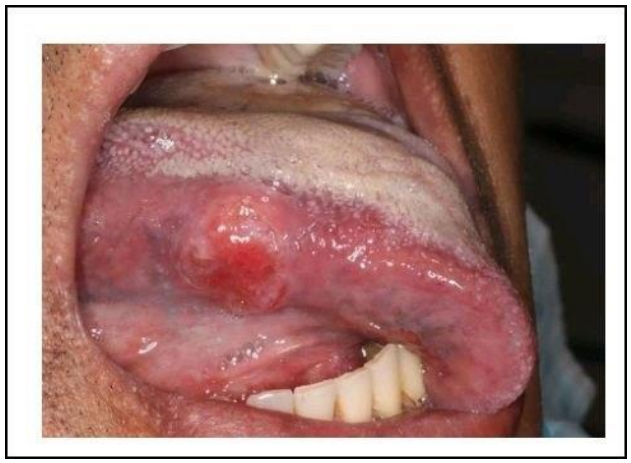

Figure 6. (Tongue) Growth-like lesion with a red ulcerative surface suspicious for OSCC

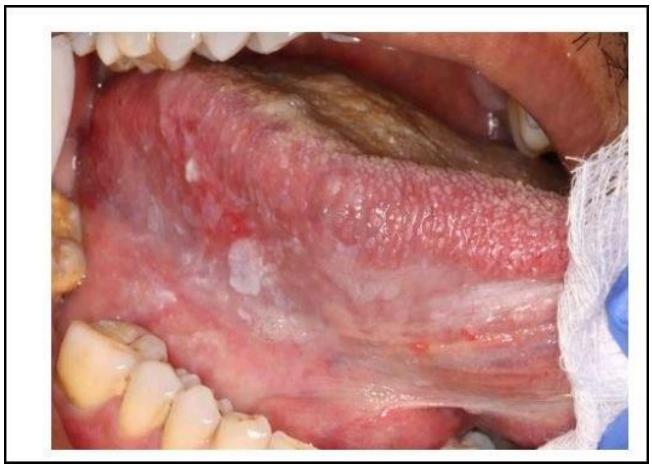

Figure 9. (Tongue) Large erythroleukoplakia suspicions for OSCC

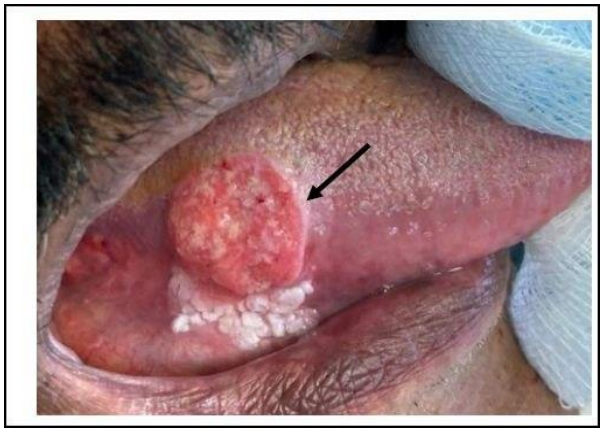

Figure 10. (Tongue) Highly suspicious growth-like lesion (arrow) presenting superior to a non-homogenous leukoplakia

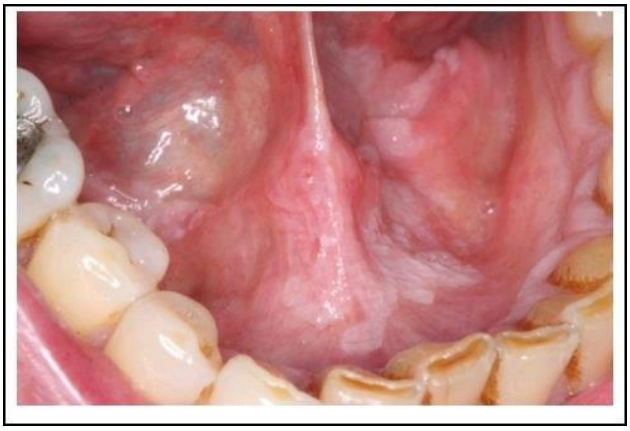

Figure 13. (Floor of mouth) High-risk non-homogenous kukoplakia

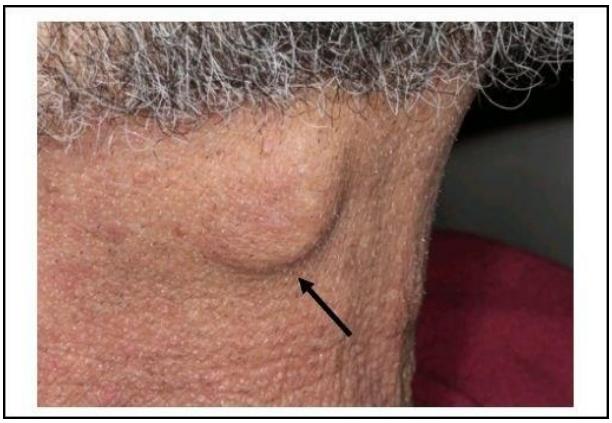

Figure 11. (Neck) Metastasis from primary oral cancer

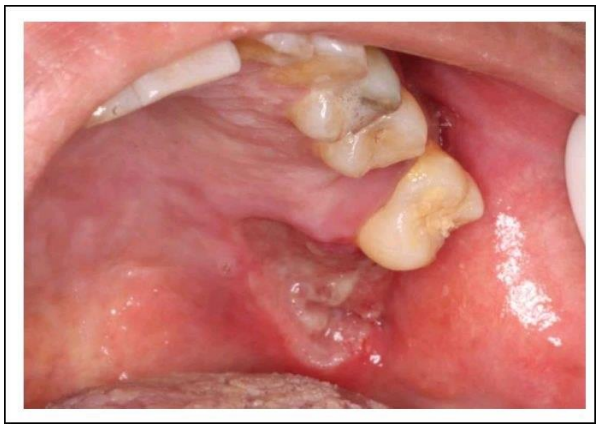

Figure 14. (Palate) A large suspicious ulcer with indurated margins and depressed alveolar mucosa

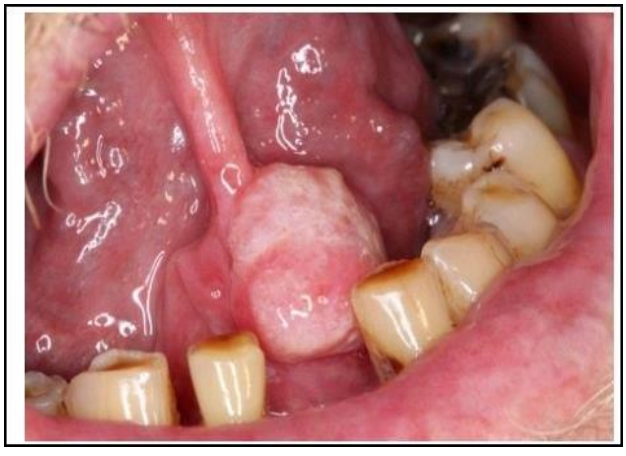

Figure 12. (Floor of mouth) Suspicious growth-like Lesion

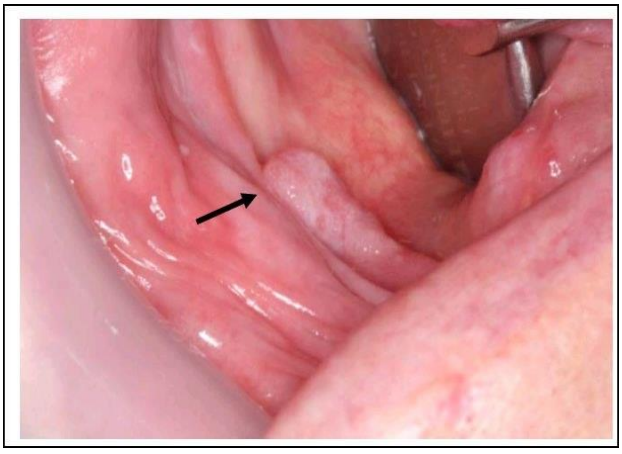

Figure 15. (Lower alveolar ridge) A soft tissue lump with irregular surface texture recently developed (arrow), suspicious for carcinoma in situ or OSCC

DIAGNOSTICS OF ORAL CANCER

Because smokers are more likely to develop oral cancer (OC), early detection is essential. A thorough patient history that identifies risk factors such as alcohol consumption, tobacco use, and HPV infection is the first step in the diagnosis process. Patients with these risks need to be examined carefully and often.

1. Toluidine Blue Vital Tissue Staining: Oral lesions are treated with a non-invasive dye. The dye is absorbed by cells with a high DNA/RNA content, which highlights potentially cancerous regions. Lugol's iodine leaves suspicious tissue unstained, while normal tissue turns brown-black. Biopsy is advised in positive areas.

2 .Optical Imaging (ViziLite, VELScope): After the patient rinses with acetic acid, blue or chemiluminescent light is used to examine the oral mucosa. When compared to healthy tissue, abnormal areas appear whiter or darker, which aids in the early detection of lesions, especially in high-risk smokers. It is not a substitute for biopsy; rather, it is an adjunct.

3. Oral Cytology (Brush Biopsy/Exfoliative Cytology): Using a brush or spatula, cells are taken from suspicious lesions. To find aberrant cells, samples are inspected under a microscope. Cytology is less specific than biopsy, which is still the gold standard, despite being less invasive.

4 .Salivary Biomarkers: Recent developments in the diagnosis of oral cancer have brought attention to salivary biomarkers' potential as a non-invasive early detection technique, which is crucial for high-risk individuals like smokers. Oral squamous cell carcinoma (OSCC) can be detected by saliva's proteins, RNA transcripts (mRNA), and other molecular markers. Interleukin-1, interleukin-8, and dual specificity protein phosphatase 1 are important markers that aid in distinguishing OSCC patients from healthy people.

For analysis, a variety of laboratory methods are used. Salivary protein levels are measured by ELISA, specific mRNA markers are found and quantified by RT-PCR, and salivary proteins can be identified with high resolution using LC-MS/MS. When combined, these techniques offer a sensitive, accurate, and non-invasive method for early diagnosis. Saliva-based diagnostics are a promising tool in oral cancer screening and prevention strategies because they provide the benefits of simple sample collection, patient comfort, and the ability to track disease progression over time. (Goldoni et al., 2021).

5-Artificial Intelligence (AI) in Diagnostics: AI examines clinical photos or cytology images to find minute mucosal alterations. In populations with limited access to specialists, machine learning and deep learning can enhance accuracy, support early detection, and identify high-risk lesions (Ahmed et al., 2021).

6. Colposcopy: Abnormal tissue and vascular changes are highlighted by a magnifying device that uses Lugol's iodine and acetic acid. Targeted biopsies can be performed on suspicious areas. Accuracy depends on operator skill.

7. Spectroscopy Biochemical or structural tissue alterations are identified by non-invasive light-based analysis. Spectroscopy can help define surgical margins during treatment and detect precancerous or early-stage lesions.

Every diagnostic technique uses advanced imaging, staining, cell collection, saliva analysis, or visualization to find suspicious oral lesions. Combining these tools with clinical examination improves early detection, especially for smokers, and directs prompt referral and biopsy (Kijowska et al., 2024).

CONCLUSION

In summary, because of its high incidence, high mortality rate, and substantial impact on patients' quality of life, oral cancer continues to be a major global health concern. The results of this study highlight how smoking, through processes like DNA damage, immunological suppression, and chronic inflammation, is one of the most important and avoidable risk factors in the onset and progression of oral cancer. When paired with additional variables like alcohol use and poor dental care, the risk is significantly raised. Smokers are at a far higher risk and typically have a worse prognosis than non-smokers, according to epidemiological studies. But quitting smoking is essential for lowering this risk and eventually enhancing clinical results. Early detection through advanced diagnostic methods, including modern imaging techniques and salivary biomarkers, is essential for improving survival rates. Therefore, implementing effective prevention strategies, raising public awareness, and promoting early screening programs are crucial steps in reducing the burden of oral cancer and enhancing patient outcomes

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