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Oropharyngeal cancer and tobacco use: Risk factors and prevention

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ABSTRACT

Oral Cancer (OC) is the most unsafe of all dental disease, while person unusual and getting little notice. It ranks 12th among all malignancies. OC has a multifaceted etiology, and much like other cancer, early recognition is critical to dropping enduring distress and boosting endurance charge. The frequency and decease rates of OC have augmented internationally, which has accelerated these study pains in the area of premature recognition and anticipation of this sickness. As an outcome, scientists have been pointed used for biopsy substitute. OC has been recognized using a diversity of molecularly based diagnostic marker, with different degree of consideration and specificity. The occurrence, humanity, risk factor, prediction, and treatment of OC are all enclosed in this paper.

Keywords: incidence and mortality, diagnostic, Oral Cancer (OC), risk factors, prevention

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INTRODUCTION

A number of different cancers, counting those of the lung, bladder, throat, esophagus, and other organs, are among the assortment of variation of this multifaceted illness that can emerge in several body regions [1]. The practice of cancer and tobacco are personally related. Many of the carcinogens included in tobacco, counting tar and benzene, can damage DNA and outcome in the increase of cancer [2]. According to estimate, smoking causes 80%-90% of lung cancer occurrence, manufacture it the main avoidable base of lung cancer. Smoking can also elevate the chance of mounting other cancers as renal, cervical cancer and pancreatic [3]. It's crucial to memorize that tobacco usage affects both smokers and non-smokers that are uncovered to used smoke. The risk of sarcoma in non-smokers is amplified by used smoke, which has many of the same cancer-causing compounds as tobacco smoke [4]. Anticipation of tobacco usage depends deeply on cultivating persons about its risk. Raising responsiveness of the danger of tobacco use is talented via health campaigns, community outreach activities and public-school initiatives [5]. Numerous army and tools, such as counselling, a replacement for nicotine, and prescription drugs, are obtainable to assist smokers stop smoking. These programmes can be very helpful to those who wish to give up smoking and reduce their chance of developing cancer [6]. Smoke-free legislation, tobacco levies, and restrictions on publicity are just a few of the policy that may assist to lower-tobacco usage. These regulations can help to create a climate that discourages tobacco use and encourage positive events [7]. The ability to avoid tobacco usage depends on having a positive atmosphere. In addition to have contact to tools like smoking termination programs, this also entails having the support of medical professionals' friends, and family [8]. The World Health Organization (WHO) states that unnecessary use of alcohol and cigarette use are two risk factor that could be banned and determine over 90% of mouth cancer occurrences [9]. In addition to lung cancer, mouth and throat cancer are the second most common cancers are shows in figure 1 caused by this addictive habit of continuous tobacco product use.

LITERATURE REVIEW

Circular miRNAs are shown to be a non-insidious biomarker for the identification of various tumours in numeral of recently published publications. Understanding biomarkers may aid in prognosis prediction and lower death rates brought on by the

discovery of novel target therapies. Table 1 provides information on the investigation of mouth cancer risk variables and preventative measures.

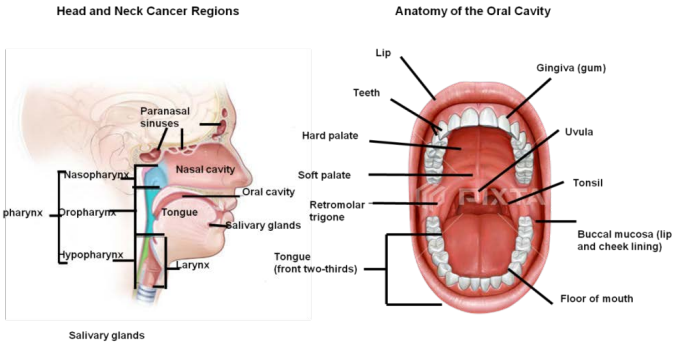

Fig. 1. Oral/mouth cancer

Tab. 1. Oral cancer risk factors and preventative techniques

Prevention Strategies	Risk Factor
Using biomarkers	Genetic predisposition
-	Precancerous lesions
-	Field cancerization
Cancer screening	Inflammation
Chemoprevention	Alcohol consumption
Anti-inflammatory drugs	HPV infection
Early detection	Oral micro biome
Probiotics	Tobacco, smokeless tobacco

Poor oral hygiene, infection with the Human Papilloma Virus (HPV), and access to specific materials and chemicals are other risk factors which could increase the growth of oral cancer. An individual's chance of acquiring OC may be considerably decreased by avoiding or limiting certain risk factors. Regular dental exams and early identification may also assist people with OC have a better outlook on life [10]. Oral cancer is mostly predisposed by tobacco use, which includes both cigarette smoking and usage of smokeless tobacco products. It's due to the fact that tobacco includes a number of dangerous chemicals and carcinogens that may destroy the cells of the mouth and throat, eventually causing cancer [11]. Because chewing tobacco and snuff are frequently kept in the mouth for extended periods of time, allowing the dangerous chemicals to come into contact with the oral tissues, they are also linked to an improved risk of oral cancer. Most crucial actions someone can do to lower their chance of acquiring mouth cancer and other significant health conditions is to stop using cigarettes [12]. In the study, epidemiology and etiology of OCC-OPC are analysed, is provided on the existing prevention strategies being used. Information was gathered from the free database maintained by the international agency for research on cancer. To describe related risk factors and prevention, literature searches were conducted [13]. The International Business Machines (IBM) Statistical Package for the Social Sciences (SPSS) Statistics 22.0 application was examining the data. 99 (50%) 3rd graders and 99 (50%) 5th graders were among the 198 dental students that participated. The majority of pupils in the 3rd and final grades reported using cigarettes (98%) and alcohol (87.4%), as well as having previously had OC lesion, viral infection, UV disclosure, chewing betel quid, being older, and eating little fruits and vegetables (85.4%). Squamish group carcinoma was identified the most prevalent type for OC both groups, when asked which lesions were more probable to be precancerous, 3rd graders fared much better than their contemporaries ($p=0.001$ and $p<0.05$). Erythroplakia and leukoplakia were properly identified as the lesions. The research made clear the value of better dental education strategies for early identification and prevention of OC [14]. One of the finest things one can due to lower cancer risk and enhance general health is to stop using cigarettes. The ability to stop smoking may be achieved at any time, and there are several tools at one's disposal, like as counselling, medicine, and nicotine replacement therapy [15]. In summary, tobacco smoking is substantial risk factor for cancer, hence avoiding an essential lowering cancer incidence. Tobacco use can be prevented and cancer rates can be lowered through education, smoking cessation programs, policy changes, and a supportive environment.

Incidence and mortality

Worldwide differences in OC prevalence and fatality rates are significant. The mortality rate is a crucial instrument that offers implied in sequence on incidence, diagnostic step, the ability of health services to solve problems, accessible technology, and to-be-implemented health initiatives, among other things. In spite of having lowest five-year the endurance excise of all tumours that are malignant, mouth cancer affects 3% of men and 2% of women worldwide. Prevalence of oral cancer in people under the age of 40 has increased by almost five times, with many cases having no identified risk factors [16]. One American each hour passes away from mouth cancer, according to research. The southern portion of India, where it is most prevalent, various locations in the east and centre of Europe, as well as a few regions of Latin America all have greater rates of OC in males than the Bas Rhin region of France. Women in India had a little rise in mortality during the 1980s and 1990s in Central and Eastern Europe. Incidence of OC has increased globally during the last several decades, according to cohort studies, especially among adolescents in countries in Eastern Europe including Estonia, Hungary, Ukraine, and Russia. New South Wales, Australia, the occurrence of OC rose by 27%

in males and 3% in women between the years 1973–1977 and 1988–1992, with the majority of the rise occurring in the early 1980s, concurrent with comparable increases in Europe and the United States. Over 75% of OC deaths in Australia occurred in adults 60 years of age or older, indicating a low risk of the disease [17]. In India, mouth cancer is up to four times more common than it is in other nations. In general, assessments are challenging since the frequency and death rates for OC are not presented in identical manner.

The risk factors

Tobacco:

Smokeless pipes, cigars, tobacco, and all other types of tobacco consumption have all been related to OC [18]. The risk of OC at all locations is enhanced by cigarette use, despite the fact that OC of the mouth floor carries the greatest risk. Ninety percent of OC fatalities in men are caused by tobacco usage.

Alcohol:

Alcohol usage is a distinct but important risk factor for the development of OC. People who don't smoke are most at risk from it. The risk increases linearly with the quantity of alcohol ingested over 30 grams per day.

Chew tobacco:

Throughout addition to smoking tobacco, chewing items including betel paan, naswar, areca chaalia, gutka, and nuts which are socially accepted throughout the South Pacific Islands, and India, and Southeast Asia, increases the risk of OC.

Shammah:

The Arabian Peninsula has a long-standing tradition of using Shammah. The average time spent applying Shammah and the development of leucoplakia are significantly correlated with one another and dose dependently [19].

Marijuana:

Cannabis usage may combine combines additional risk factors and mutagen sensitivity can increase the chance of head and neck cancer. Marijuana smoke has similar cancer-causing qualities as cigarette smoke.

Poor nutrition:

Nutritional deficiency, generally those iron, selenium, folate, vitamin A, C and E and levels of other components, is associated to an improved risk of OC [20]. Nutritional deficits, including those of iron, selenium, folate, vitamin A, C, and E, as well as levels of other nutrients, have been associated with a higher risk of OC.

Ultraviolet light:

Exposure to sunlight is an essential risk factor for growing lip cancer. Lower lip cancer most often develops, and a lot of individuals work outside where their exposure to sunlight is higher [21]. Men are twice as probable as women to get lip cancer, which could be related to profession, smoking, and being in the sun.

Irritation:

The majority of research has shown no connection between OC and the persistent irritation to the oral mucosa caused by ill-fitting or faulty full dentures, despite some speculation to the contrary.

Dental plaque:

Oral health could be another factor in the growth of OC because polymicrobial the supragingival oral plaque has a meaningful mutagenic interaction with saliva, making it a potential autonomous risk factor.

Mouth rinses:

To mouthwashes, ethanol is used as a preservative and a solvent for additional components. A study demonstrates that using mouthwash while abusing alcohol or cigarettes has no statistically significant connection to cancer [22]. Ethyl alcohol contained in mouthwashes does not currently seem to be associated with OC due to a lack of solid clinical data.

Candidacies:

Multi-endocrine system autoimmune disease a limited T- lymphocyte deficit-related autosomal recessive condition known as candidiasis-ectodermal dystrophy, which predisposes to chronic mucositis and OC, is exceptionally common in Finland and appears to be exacerbated by *Candida albicans.*

Diabetes:

Glucose transmitter substrate-1 and the focal adhesion could be involved in the molecular foundation for the hypothesized correlation between Oral Squamous Cell Carcinomas (OSCC) and diabetes mellitus demonstrated by epidemiological studies.

Free radicals:

Oxidative damage, which includes Reactive Oxygen Species (ROS) and Reactive Nitrogen Species (RNS), has the power start and encouraging growth of cancer. Antioxidants prevent the cellular and molecular damage that these unstable molecules may cause [23]. It is conceivable that enhance in ROS and RNS was the source of consumption and depletion of aqueous antioxidant systems, which would help to explain the oxidative damage to the DNA the potential promotion of OC.

Viruses:

The most compelling reason points to a disease with high-possibility HPV. Studies demonstrate a higher incidence of OC among women with cervical cancer, which points to an additional risk factor outside smoke, such as HPV disease. According to a recent multicentre case-control research, HPV-16 infection raised the risk of oral cancer, especially or pharyngeal carcinoma [24]. Herpes Simplex Viruses (HSV) and the Epstein-Barr virus infection still play an unknown part. It has also been investigated how the herpes simplex virus HSV-1 and HSV-2 interact HPV-16 infection, cigarette usage, and alcohol consumption. While being seropositive for HSV-1 and HSV-2 can alter the likelihood of being exposed to alcohol, cigarettes, or HPV, heavy use has been linked to a persistently elevated risk of OSCC even as people age, alcohol consumption, and nicotine usage into consideration. HPV disease was related to OC in research that used fuzzy logic.

Family history:

An OC diagnosis in the family is a risk factor. Chromosome damage from pollutants is more probable to occur in head and neck cancer patients. In a study use cDNA array, it was shown that the term of certain genes was altered in the neck and head region SCC tissues compared to typical tissue [25].

Prevention of oral cancer

Primary obstacle:

According to estimates, primary obstacle is the most economical strategy for avoiding OC. Poor public knowledge of OC has been shown by prior research. By eliminating environmental factors, particularly excessive alcohol and cigarette use, up to three-quarters of OC may be avoided.

Secondary prevention:

Leukoplakis and erythroplakias are treated and removed, together with risk factors linked to their formation; to lower the occurrence of OC. Patients' routine checkups might include opportunistic screening for OC [26]. A professional should be seen for a clear diagnosis, a biopsy, and subsequent care if the patient has positive results.

Current experimental models:

The examination of carcinogenesis and the establishment of diagnostics, many experimental models have been utilized. Treatment with 4-nitroquinoline 1-oxide in drinking water has been shown to cause tumours in mouse oral cavities and rat tongue carcinogenesis. Nitric Oxide (NO) also contributes significantly to the development of tumours and carcinogenesis. In rat tongue cancer caused by 4-NQO, iNOS expression was shown to be considerably greater.

Current oral cancer diagnostic:

The traditional and most widely used diagnostic techniques for precancerous and cancerous oral lesions include clinical assessment and histological analyses of biopsied material. Traditional oral examinations may be helpful in identifying certain oral lesions, but they do not always reveal any lesions that might be cancerous or organic [27]. On the other hand, biopsy is a method that may have surgical repercussions, professional restrictions in terms of skill, and patient-specific psychological repercussions. Formal diagnostic processes don't start until the doctor or patient sees abnormal tissues since the majority of OCs develop as tiny, asymptomatic lesions. Additionally, because imaging techniques are time and money consuming, they are not practical for cancer screening. Due to their insensitivity for small lesions, these techniques are typically employed for confirmation. Scientists have been looking for alternatives in light of this. In this sense, the cytokeratin expression profile offers helpful data on the state of cell differentiation, nonetheless, its capacity for early OC detection is restricted [28]. Additionally, some cytokeratin's, such K8 and K19, might be useful, although not conclusive, markers of malignancy, especially when their presence is interpreted in combination with additional data, like a DNA report. Another prevalent genetic alteration in human malignancies is a mutation of the tumour suppressor DNA p53. The majority research indicates that although p53 is not there in healthy oral mucosa, it may be found using immunohistochemical techniques in SCCs and other possibly cancerous lesion of the mucosa of the mouth. The p53 gene has also been found in cell taken from cancerous tumours by exfoliative cytology. Additionally, p53 mutations are only detected at advanced stages of carcinogenesis and are found in only 50% of oral cavity squamous cell carcinomas. Since exfoliative cytology does not produce basal epithelial cells, early diagnosis of OCs is not a practical approach based on the detection of p53 in oral mucosa smears. Exfoliative cytology has grown in significance as a quick and easy way to collect DNA samples, and molecular techniques have substantially replaced histopathological procedures in the diagnosis of disease. In exfoliated cells, Loss of Heterogeneity (LOH) and other molecular alterations suggestive of oral carcinogenesis are easily seen. To investigate Restriction-Fragment Length Polymorphisms (RFLPs) in exfoliation samples from oral carcinomas, Polymerase Chain Reaction (PCR) techniques have been utilised [29]. They discovered that 66% of the tumours had LOH at a single place in the p53 sequence, compared to 55% of the tumours that had LOH at several locations. While leukoplakia is suggestive of an elevated risk of OC, neither clinical nor histological markers are reliable for predicting whether the lesion would heal spontaneously or develop into cancer. Oral leukoplakia can benefit from the use of chemo preventive medications with new molecular targets found via microsatellite research. By encouraging the invasive, angiogenic, and migratory properties of cancer cells which can also be triggered by the activation of cyclooxygenase-2—NO can aid in the growth and spread of cancer. Recently, the involvement of COX-2 in the development of cancer has received a lot of attention. Additionally, it is widely expressed in OC and oral premalignant lesions and seems to be particularly enhanced in high-risk oral lesions [30]. It was demonstrated that the human OSCC has much greater iNOS expression. Therefore, the development of OC can be significantly impacted by the NO produced by iNOS. Saliva is a widely accepted, superior early illness indicator that improves treatment outcomes, a means of assessing risk for systemic and oral diseases down the road, and a straightforward, non-invasive substitute for blood and urine tests. Prior to beginning treatment, individuals with OSCC had their salivary Endothelin-1 (ET-1) levels assessed. The findings indicated that the OC had considerably greater ET-1 levels than the controls, indicating that individuals who are at risk for OC may benefit from monitoring their salivary ET-1 levels. Moreover, antioxidant enzyme identification can eventually prove to be a helpful marker for the molecular diagnosis of the OC.

Analysis

Smokeless tobacco use:

An estimated 8.7 million individuals, or 3.3% of those aged 12 and over, used smokeless tobacco in 2014. In the previous month, men were more likely than females to have used smokeless tobacco [31]. According to figure 2, 13% of women and 36% of men in 2020 reported using smokeless tobacco in the previous month. Young adults (18 to 25 years old) were more likely than adolescents (12 to 17 years old) and adults (26 and older) to have used smokeless tobacco in the month prior. According to these statistics, 15% of users are between the ages of 12 and 17, 16% million are among the ages of 18 and 25, and 20% of users are older than 26.

About age at start, extent, and occurrence of chewing a day, linear dose-response organization was found connecting chewing tobacco use oral cancer. As shown in figure 3, risk of oral cancer was improved by smoking more than 10 cigarettes per day and over a period longer than 25 years.

Indian oral cancer mortality rate

In India, oral cancer is one of the top three malignancies to be diagnosed, and in certain regions, it is the leading cause of cancer-

related death [32]. Annually, there are about 70,000 new cases and more than 48,000 fatalities brought on by oral cancer. Oral cancer is the second most prevalent disease in males and the fourth most common in women, accounting for up to 20% of cancer diagnoses in much of India shown in figure 4 and table 2. But those GLOBOCAN statistics for the entirety of India are extrapolations based on information from regional cancer registries and the nation's estimated population. The instances that are reported vary significantly amongst registries, as will be seen from this transcript.

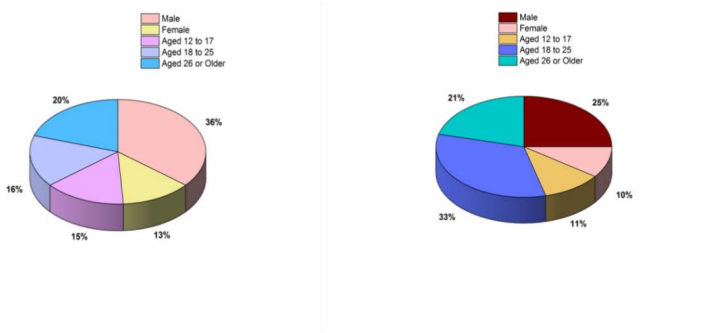

Fig. 2. Smokeless tobacco consumption by gender and age group in 2020

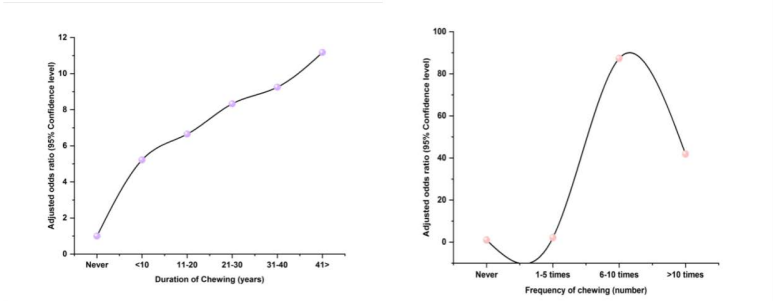

Fig. 3. Association between frequency and duration of chewing tobacco and incidence of oral cancer

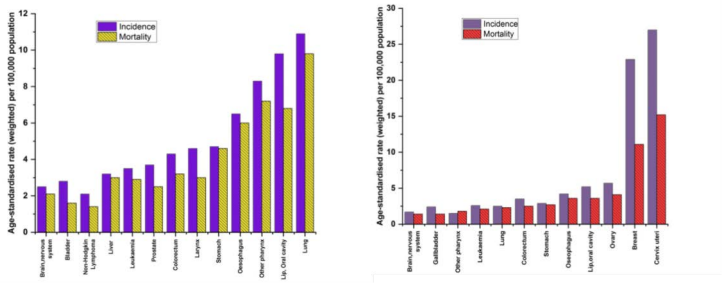

Fig. 4. Most frequent cancers among males and females in India according to GLOBOCAN data

Tab. 2. National cancer mortality estimated

	Age-Standardized Rate (Weighted) Per 100,000 Population	
Brain, Nervous System	2.5	2.1
Bladder	2.8	1.6
Non-Hodgkin Lymphoma	2.1	1.4
Liver	3.2	3
Leukaemia	3.5	2.9
Prostate	3.7	2.5
Colorectum	4.3	3.2
Larynx	4.6	3
Stomach	4.7	4.6
Oesophagus	6.5	6
Other Pharynx	8.3	7.2
Lip, Oral Cavity	9.8	6.8
Lung	10.9	9.8

Brain, Nervous System	1.7	1.4
Gall Bladder	2.4	1.4
Other Pharynx	1.5	1.8
Leukaemia	2.6	2.1
Lung	2.5	2.3
Colorectum	3.5	2.5
Stomach	2.9	2.7
Oseophagus	4.2	3.6
Lip, Oral Cavity	5.2	3.6
Ovary	5.7	4.1
Breast	22.9	11.1
Cervix Uteri	27	15.2

CONCLUSIONS

The most potentially fatal dental ailment is OC. Unfortunately, the majority of Invasive cancers of the mouth are not detected until they have progressed significantly. This dismal prognosis is essentially caused by the fact that the majority of patients arrive with a diagnosis of an advanced illness. The pathologist's subjectivity is one of the most crucial aspects of the biopsy research, despite the fact that it is a basic diagnostic technique with low sensitivity. Novel diagnostic and prognostic approaches, together with patient monitoring in oral precancer and cancer, have recently attracted renewed interest. Furthermore, OC has been detected using a range of molecular-based diagnostic markers, each with varying degrees of specificity and sensitivity. However, none of the oral cavity's malignant lesions have any specific tumoral markers present. Moreover, research has shown that the risk of oropharyngeal cancer increases with the duration and intensity of tobacco use. The risk is also higher for individuals who use both tobacco and alcohol. In conclusion, tobacco use is a major modifiable risk factor for oropharyngeal cancer. Therefore, efforts to reduce tobacco use, such as public health campaigns and smoking cessation programs, are essential in preventing the development of this type of cancer. Additionally, regular screening and early detection of oropharyngeal cancer can improve the prognosis and increase the chances of successful treatment.

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