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Original Research Article

ASSOCIATION OF ORAL CANCER WITH CONSUMPTION OF TOBACCO, SMOKING AND ALCOHOL: A PROSPECTIVE COHORT STUDY OF HOSPITAL PATIENTS

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Abstract

Background: Oral cancer is a type of malignant neoplasia that develops in the tissues of lips or oral cavity. Oral cancer is a significant contributor to global mortality, and despite treatments, the 5-year survival rate remains at approximately 50%. Epigenetic modifications are thought to play a critical role in the development of oral cancer through various mechanisms such as changes in histone modification, aberrant DNA methylation, and dysregulation of miRNA expression. **Materials and Methods:** The study was conducted in department of pathology, GSVM Medical College, Kanpur Nagar, Uttar Pradesh, India among 800 patients from June 2022 to November 2022.The patients were explained about the study and confidentiality of data was ensured. Patient being diagnosed with any kind of dysplasia (Mild/Moderate/Severe), leukoplakia and carcinoma in situ were included in this study. Descriptive statistics were utilized to present general data. **Result:** In present study, we monitored a group of individuals over a period of time and found a notable correlation between the onset of oral cancer and the use of tobacco, smoking, and alcohol consumption. **Conclusion:** According to our findings, we suggest that individuals who are 30 years old or above and habitually smoke cigarettes, consume alcohol, or use tobacco should undergo periodic oral mucosa screenings to identify any possible onset of oral cancer at the earliest. It is imperative to emphasize that early detection plays a vital role in effectively treating oral cancer and achieving favourable outcomes for patients.

INTRODUCTION

Oral cancer is a type of malignant neoplasia that develops in the tissues of lips or oral cavity. It is typically classified as a squamous cell carcinoma (OSCC), as 90% of cancers in the oral region are histologically derived from squamous cells.[1] This type of cancer can vary in terms of differentiation and has a tendency to spread to the lymph nodes. Oral cancer is a significant contributor to global mortality, and despite treatments, the 5-year survival rate remains at approximately 50%.[2] Epigenetic modifications are thought to play a critical role in the development of oral cancer through various mechanisms such as changes in histone modification, aberrant DNA methylation, and dysregulation of miRNA expression.[3] These modifications can lead to altered gene expression patterns and disruption of important cellular processes, ultimately contributing to the development and progression of oral cancer. Understanding the role of epigenetic modifications in oral carcinogenesis may lead to the development of new therapeutic strategies and improved outcomes for patients [Figure 1].[4-6]

Oral cancer is the most frequent form of cancer in India, responsible for 50 to 70 percent of all cancer deaths, and it has the highest rate of incidence among Asian nations.[7-10] Oral cancer is ranked as the sixth most prevalent type of cancer globally.[11-14] It can affect various parts of the oral cavity, including the anterior tongue, cheek, floor of the mouth, gingiva, and other regions. There is a significant variation in the global occurrence of oral cavity cancer. While it accounts for less than 5% of all cancers in countries such as the United States, Australia and Western Europe and some regions such as India, certain areas in Brazil, France, and

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Central and Eastern Europe have among the highest rates of oral cavity cancer in world. The regional differences in the incidence of oral cancer can likely be attributed to varying social customs. Historically, the high rate of oral cancer in France and Eastern Europe has linked to the excessive consumption of alcohol and tobacco in this region.[15-18]

The practice of chewing betel nut leaves combined with lime and tobacco, commonly referred to as pan which results in prolonged exposure of the carcinogen to the buccal mucosa.[19,20] This extended contact is believed to be the primary reason of oral cancer in India. The incidence of oral cancer is positively correlated with the age of the individual.[21.22] The rates show a steep increase after the age of 40 to 49 years, reaching a plateau around 70 to 79 years as shown in [Figure 2]. As a result of the growing aging population in most countries worldwide, even if the current age-specific rates remain unchanged, there will be a rise in the adult population with an increased risk of oral cancer. Men are more prone to developing oral cancer than women, and the risk is between two to six times higher in males depending on the location of the cancer within the oral cavity. This increased risk in men is largely attributed to their higher consumption of tobacco and alcohol.[23]

Etiology and Major risk Factors

The two primary factors that impact most diseases are genetic and epigenetic factors. The development of oral carcinoma is influenced by a combination of these factors, including tobacco and alcohol consumption, diet and nutrition, radiation, viruses, ethnicity, familial and genetic predisposition, immune-suppression, oral thrush, syphilis, use of mouthwash, dental factors, occupational risks, and mate [Figure 3].[2-25]

Epigenetic Factors

Tobacco

The leading risk factor for cancer remains tobacco consumption, which is accountable for millions of cancer-related deaths annually. Smoking is linked to various neoplastic diseases, including those affecting the lung, pharynx, oral cavity, esophagus, larynx, urinary bladder, pelvis, kidney, and pancreas. Epidemiological studies have firmly established a strong correlation between smoking and oral cancer.[26,27] Smoking is the most prevalent form of tobacco use and is delivered through various methods such as cigarettes, cigars, pipes, bidis, and hookahs or chillums (a type of clay pipe used to smoke burning tobacco). Hookah or chillum smoking is also a common practice in some Asian countries, including India. Moreover, some parts of India, such as Mizoram, have a unique form of tobacco use where tobacco smoke is dissolved in water, known as "smoke on the water".[28-32]

Exposure of carcinogens, such as tobacco smoking is responsible of alteration of crucial biological pathways. These pathways include genetic mutations, immune disorders, oxidative stress, epigenetic changes, as well as virus induced alterations in signalling pathways and cellular metabolism.[32,33] [Figure 4] presents an overview of the potential pathways that can lead to smoking associated carcinogenesis. Understanding these pathways is critical in developing effective prevention and treatment strategies for oral cancer.

The most significant carcinogens found in tobacco smoke are the aromatic hydrocarbon benz-pyrene and the tobacco-specific nitrosamines, which include 4-(nitrosomethylamino)-1-(3-pyridyl)-1-butanone (NNK) and N'-nitrosonornicotine (NNN) 6. Animal studies have demonstrated that the tobacco-specific nitrosamines NNK and NNN found in tobacco products have the capability to cause malignant neoplasms in various parts of the body such as the oral cavity, lung, esophagus, and pancreas. This is because NNK, NNN, and their metabolites have the ability to bind covalently with the DNA of keratinocyte stem cells, leading to the formation of DNA adducts.[2,27] The DNA adducts caused by NNK, NNN and their metabolites are crucial in inducing DNA replication mutations. The transformation of these carcinogens involves oxidation through the action of P450 enzymes in cytochromes and conjugation through the activity of glutathione-S-transferase (GST). The genetic predisposition to head and neck cancers induced by tobacco consumption is thought to be strongly influenced by genetic variations in the genes that code for enzymes involved in the metabolism of carcinogens present in tobacco products. These enzymes include P450 enzymes in cytochromes and glutathione-S-transferase (GST).[17,28]

Erroneous metabolism of carcinogens may lead to increased exposure and make individuals more susceptible to cancer. This is because certain polymorphic xenobiotic metabolizing enzymes (XMEs) are involved in the activation or degradation of carcinogens and procarcinogens, and they strongly impact an individual's biological responses to carcinogens. XMEs, which are predominantly located in the liver, are also present in the mucosa of the upper aerodigestive tract. Several of these enzymes exhibit polymorphic traits. Many research studies shows that tobacco interferes with the xenobiotic metabolism, hence, may result in increased susceptibility to cancer.[29-33]

The consumption of smokeless tobacco, in which tobacco is placed inside the oral cavity without being burned, has become widespread globally. This method of consuming tobacco allows nicotine to be absorbed through contact with the mucous membranes in the oral cavity, thereby producing the desired effect. Smokeless tobacco, which is consumed without combustion, is utilized globally in various forms.[34] For example, the use of oral snuff (moist or wet snuff) is widely practiced in the Western world and the Middle East.[35] In Asia, betel quid chewing, in different styles and composed of various components, is prevalent and has been a cultural tradition since tobacco was introduced to India by the Portuguese, who brought it to Europe

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and Asia from South America. Smokeless tobacco, consumed without burning, has various forms of use worldwide. Its consumption primarily results in oral precancer and cancer.[36] The consumption of plug, loose-leaf, and twist chewing tobacco is decreasing in Western Europe and North America, except for certain groups 42. In North America and Scandinavia, moist snuff made from ground tobacco is increasingly popular. However, oral snuff usage, also known as "snuff-dipping," has been associated with "snuff-dipper's cancer," a form of verrucous carcinoma that is caused by snuff consumption.[12,13]

Alcohol

Several studies have confirmed the role of alcohol as a risk factor for oral cancer (OC). However, there is debate regarding the potential carcinogenic impact of alcohol alone due to the fact that many epidemiological studies have involved subjects who simultaneously consumed both alcohol and tobacco.[37] Individuals who consume more than 170 grams of whiskey on a daily basis have been shown to have a ten-fold higher risk of oral cancer compared to those who consume smaller amounts. It has been shown that it increases the uptake of carcinogens into the cells that are exposed, changing the metabolic processes of the oral mucosal cells.[38] Alcohol may have an additive effect, studies have demonstrated that the combined consumption of alcohol and tobacco increases the risk of oral cancer compared to using either substance alone. However, limited studies have been conducted to examine the individual impact of either alcohol or tobacco on oral cancer risk, particularly in patients who only consume one of the two substances. In a study conducted among an Indian population, it was determined that alcohol consumption is a standalone risk factor for oral leukoplakia.[39] However, investigations evaluating the presence of oral epithelial dysplasia in individuals who consume alcohol but do not smoke have revealed that the significance of alcohol in the development of oral epithelial dysplasia is only established when taken into consideration alongside the use of tobacco.[40] There was no evidence to support the correlation between heavy smoking or heavy alcohol consumption and minor salivary gland tumors. As a result, the independent impact of alcohol on oral carcinogenesis remains uncertain, although numerous epidemiological studies support its synergistic effect when consumed with tobacco. Alcohol has been shown to increase the permeability of oral mucosa, causing morphological changes such as epithelial atrophy that increase the penetration of carcinogens into the oral mucosa.[41]

Alcoholic drinks contain a variety of cancer-causing substances, such as N-nitroso compounds, mycotoxins, urethane, and inorganic arsenic. The primary metabolic product of alcohol, acetaldehyde, is broken down by the alcohol dehydrogenase (ADH) enzyme. Subsequently, the enzyme aldehyde dehydrogenase (ALDH) oxidizes acetaldehyde to acetate. Studies indicate that acetaldehyde can harm DNA in cultured mammalian cells by interfering with DNA synthesis and repair, triggering sister chromatid exchanges and causing specific gene mutations.[42-44] Acetaldehyde also hinders the function of 6-methylguanine transferase, a vital enzyme that repairs damage caused by alkylating agents. This substance has various negative impacts, including promoting tumor growth. When acetaldehyde builds up in the body due to heightened production or diminished elimination, it can have harmful effects. This build-up can result from heightened activity of the ADH enzyme found in oral microflora and the oral mucosa. Individuals who possess ADH type-3 genotypes have a rapid oxidation process of alcohol to acetaldehyde and are therefore at a greater risk for oral cancer. On the other hand, a reduction in the ALDH enzyme can also result in an accumulation of acetaldehyde. There have been reports of genetic variations in both the ADH and ALDH enzymes, which have been linked to an elevated danger of cancers associated with alcohol consumption. The systemic consequences of alcohol consumption are primarily caused by liver damage. Alcoholism, which can lead to conditions such as cirrhosis and other ailments like cardiomyopathy, stroke, and dementia, impairs the body's ability to detoxify carcinogenic substances such as N-nitrosodiethylamine. Chronic alcoholism results in decreased intake of essential nutrients due to the metabolic processes being occupied with transforming ethanol. This leads to alterations in proper nutrient metabolism and increases the danger of nutritional deficiencies, thereby raising the likelihood of cancer. Chronic alcohol consumption also undermines the immune system by impacting the liver and nutritional state.[45-47]

Despite efforts to improve the treatment of oral cancer, there has not been a major breakthrough in recent years. While a multidisciplinary approach that integrates different therapeutic approaches has improved the quality of life for oral cancer patients, the 5-year survival rate has remained relatively unchanged in recent decades. Consequently, it is crucial to implement primary preventive measures, such as quitting tobacco use and alcohol consumption, along with early detection strategies, in order to enhance the outlook for oral cancer patients.

There have been limited prospective cohort studies that have analyzed the risk factors associated with the development of oral cancer. This study aimed to fill this gap by exploring the connection between oral cancer and the behaviours of smoking and consuming alcohol in a prospective manner. Additionally, the study aimed to explore the combined impact of these behaviours on oral cancer risk.

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MATERIALS AND METHODS

Literature Search

To conduct the literature review for this study, the NCBI Pubmed database was searched using specific keywords such as "oral cancer", "risk factor", "epidemiology", and "patho*". In addition to this, relevant information was obtained from medical university websites and textbooks.

Study Design

This study was conducted in department of pathology, GSVM Medical College, Kanpur Nagar, Uttar Pradesh, India among 800 patients from June 2022 to November 2022. The patients were explained about the study and confidentiality of data was ensured. Patient being diagnosed with any kind of dysplasia (Mild/Moderate/Severe), leukoplakia and carcinoma in situ were included in this study (Figure 5). The participants were initially requested to elaborate on their individual practices concerning tobacco and alcohol consumption over the past half-year. Individuals who indulged in the use of tobacco or alcohol only on occasional events such as weddings, family gatherings, or birthday celebrations were not considered as frequent users. Subsequently, a visual examination of the oral cavity was conducted using appropriate lighting and instruments. Any oral cavity lesion that was present for more than 2 weeks and appeared as a non-healing ulcer, persistent white or red lesion, easily bleeding lesion or an uneven surface was regarded as a positive outcome. Once an explanation was provided, a punch biopsy of any anomalous lesion was performed. If the patient had any reservations about undergoing further biopsy, follow-up was strongly advised.

Statistical Analysis

In this study, descriptive statistics were utilized to present general data. The Chi-square test was employed to compare nominal or ordinal variables between oral cancer patients and non-oral cancer patients. Furthermore, the logistic regression model was used to analyze the crucial factors that contribute to the contraction of oral cancer. SPSS for Windows, version 10.1 (SPSS Inc., Chicago, IL, USA), was used to perform the statistical analysis. A statistical significance level of $P<.05$ was considered significant.

RESULTS

In present study 800 patients data was included. These patients include 613 male and 187 female. The ages ranged from 10 to 90 years. Maximum numbers of participants fall in the age group of 41-50 years, followed by 31-40 years age group. Results of statistical analysis of male patients are summarised in [Table 1]. Total patient investigated in this study contains 76.66% male out of which 92.33% have oral cancer. 72.43 % male patients use tobacco out of which 90.99 % have oral cancer. Tobacco and alcohol consumption consist of 5.05% in which 100% have oral cancer. In case of tobacco & smoking consumption, 9.46% of male population of study is involved, and in which 94.82% have oral cancer. Only smoking, only alcohol and smoking & alcohol male population of this study is 1.63%, 0.16 % and 0.655% respectively, further oral cancer patients in these all cases are 100%. Tobacco, smoking & alcohol consuming population in study subject are 10.6%, and out of which 93.84% having active oral cancer.

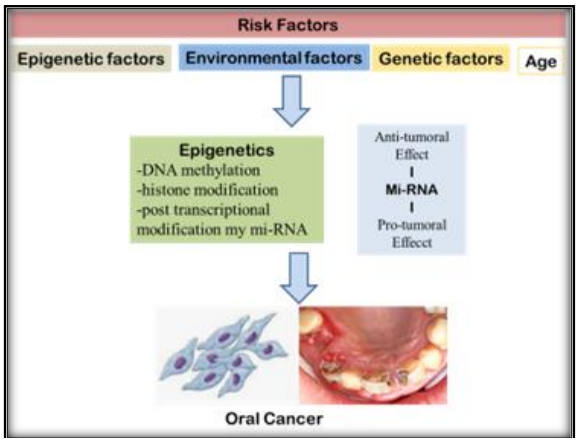

Figure 1: Various risk factors associated with oral cancer

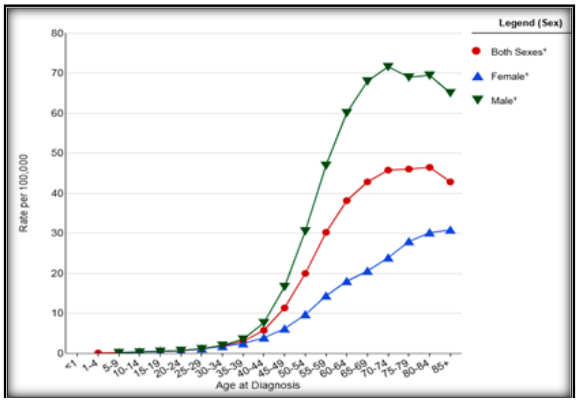

Figure 2: Incidence of cancer of Oral Cavity and Pharynx (Source with courtesy: SEER Explorer https://seer.cancer.gov/statistics-network/explorer/.)

Figure 3: Oral Cancer risk factor

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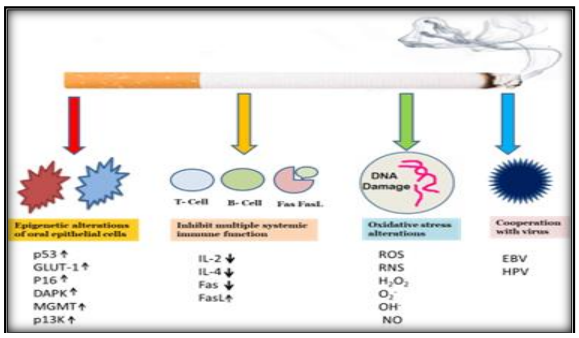

Figure 4: An overview of potential pathways involved in oral carcinogenesis

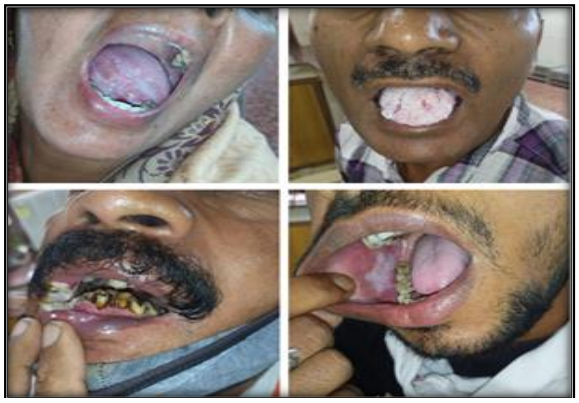

Figure 5: Various oral cancer sites observed during present study

Results of statistical analysis of female patients are summarised in [Table 2]. Total patient investigated in this study contains 23.37% female out of which 89.83% have oral cancer. 96.79 % female patients use tobacco out of which 89.50 % have oral cancer. Tobacco & alcohol consumption consist of 0.534 % in which 100% have oral cancer. In case of tobacco & smoking consumption 2.13% of female population of study is involved, and in which 100% have oral cancer. Only smoking, only alcohol and smoking & alcohol female population of this study is 0.534%, 0 % and 0% respectively. Further, oral cancer patients in case only smoking is 100%. Oral cancer occurrence in tobacco, smoking & alcohol consuming female population is 0%.

Bivariate Analysis

Male and female patients are divided in separate groups, and they are further divided in the patients with oral cancer and without oral cancer. Total participants in this study are 800. Among them participants 734 have oral cancer. Further all participants are divided in male and female groups and there are variables are summarised in [Table 1 and Table 2]. Chi square test of significance have been applied between different variables and we observed the significant difference between different variables summarized in [Table 1 and Table 2].

Table 1: Descriptive and bivariate analyses of male population.

Variables	Total No. of patients (800)	Oral cancer		P Value
		Yes (No. of patients)	No (No of patients)	
Males	613 (76.66%)	566 (92.33%)	47 (7.66%)	
Only tobacco use				
Yes	444 (72.43%)	404 (90.99%)	40 (9.00%)	< 0.05
No	169 (27.56%)	162 (95.85%)	7 (4.14%)	
Tobacco & Alcohol				
Yes	31 (5.05%)	31 (100%)	0 (0%)	< 0.05
No	582 (94.61%)	535 (91.92%)	47 (8.07%)	
Tobacco & Smoking				
Yes	58 (9.46%)	55 (94.82%)	3 (5.17%)	< 0.05
No	555 (90.53%)	511 (92.07%)	44 (7.92%)	
Only smoking				
Yes	10 (1.63%)	10 (100%)	0 (0%)	< 0.05
No	603 (98.36%)	556 (92.20%)	47 (7.79%)	
Only alcohol				
Yes	1 (0.163%)	1 (100%)	0 (0%)	< 0.05
No	612 (99.83%)	565 (92.32%)	47 (7.67%)	
Smoking & Alcohol				
Yes	4 (0.652%)	4 (100%)	0 (0%)	< 0.05
No	609 (99.34%)	562 (92.28%)	47 (7.71%)	
Tobacco, Smoking & Alcohol				
Yes	65 (10.60%)	61 (93.84%)	4 (6.15%)	< 0.05
No	548 (89.39%)	505 (92.15%)	43 (7.84%)	

Table 2: Descriptive and bivariate analyses of female population

Variables	Total No. of patients (800)	Oral cancer		P Value
		Yes (N of patients)	No (No of patients)	
Females	187 (23.37%)	168 (89.83%)	19 (10.16%)	
Only tobacco use				
Yes	181 (96.79%)	162 (89.50%)	19 (10.49%)	< 0.05
No	6 (3.20%)	6 (100%)	0 (0%)	
Tobacco & Alcohol				
Yes	1 (0.534%)	1 (100%)	0 (0%)	< 0.05
No	186 (99.46%)	167 (89.78%)	19 (10.21%)	
Tobacco & Smoking				

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Yes	4 (2.13%)	4 (100%)	0 (0%)	< 0.05
No	183 (97.86%)	164 (89.61%)	19 (10.38%)	
Only smoking				
Yes	1 (0.534%)	1 (100%)	0 (0%)	< 0.05
No	186 (99.46%)	167 (89.78%)	19 (10.21%)	
Only alcohol				
Yes	0 (0%)	0 (0%)	0 (0%)	< 0.05
No	187(100%)	168 (89.83%)	19 (10.16%)	
Smoking & Alcohol				
Yes	0 (0%)	0 (0%)	0 (0%)	< 0.05
No	187 (100%)	168 (89.83%)	19 (10.16%)	
Tobacco, Smoking & Alcohol				
Yes	0 (0%)	0 (0%)	0 (0%)	< 0.05
No	187 (100%)	168 (89.83%)	19 (10.16%)	

DISCUSSION

The notable rise in tobacco and alcohol consumption per person has been identified as a possible contributor to the surge in oral cancer in various regions worldwide, including India.[5] The annual production of tobacco in India has been consistently growing over the years, and this trend correlates with the rapid increase in oral cancer cases in the country. As a result, oral cancer prevention has emerged as a major public health concern in India.

Oral cavity cancer is strongly linked to tobacco use, smoking and alcohol consumption. While these risk factors are widely recognized, most of the relative risk estimates associated with them have been derived from case-control studies.[4] In this work, we aimed to overcome the selective bias which often arises in case-control studies by conducting a prospective cohort study. This type of study design allowed us to observe and track individuals over time, providing more reliable and accurate data on the potential risk factors associated with oral cancer.

In this hospital based study, a total of 800 individuals underwent oral cavity examination for cancer, and 734 participants (91.75%) were diagnosed with oral cancer pathologically. The discrepancies between the findings of this study and previous studies may be attributed to differences in the characteristics of the populations being studied. Among those identified as having abnormal lesions in this study, all participants underwent a biopsy, and 734 of them were ultimately diagnosed with malignancies. As a result, the positive predictive rate (the proportion of individuals with abnormal lesions who were confirmed to have cancer through biopsy) of present study was 91.75%, which is similar to that reported in other similar case studies.

In this study, the rate of tobacco use and smoking was discovered to be 9.46%, aligning with the rates documented in earlier studies. Similarly, the prevalence of tobacco use, smoking and alcohol consumption observed in this study is comparable to those reported in earlier research conducted in India. Interestingly, we observed high privilege of smokeless tobacco mainly gutkha consumption, in males (72.43%) as well as in females (96.76%). This finding is also correlated with the fact that Kanpur district is birth place of gutkha as well as main industrial production site of gutkha in central India. Further this finding also suggested that in female mainly consumed tobacco in smokeless form. These gutkha consuming individuals were at the high risk of occurrence of oral cancer as suggested in this study. 90.99% of male and 89.50% of female consuming gutkha shows pathologically proven oral cancer. Further, the study shows that other variables are not so strongly correlated with oral cancer in both males as well as in females.

Tobacco is a known source of N-nitroso compounds, which are recognized carcinogens and responsible for development of oral cancer. In addition to N-nitroso compounds, tobacco also contains other carcinogens such as 4-(methylnitrosoamino)-1-(3-pyridyl)-1 butanone (NNK) and polycyclic aromatic hydrocarbons (PAH). These harmful substances have the ability to cause specific mutations, especially G:T transversions, which are changes in the genetic code that can lead to the development of cancerous cells. Therefore, tobacco use can significantly enhance the risk of oral cancer occurrence due to its carcinogenic components.[16,21]

Long-term exposure to carcinogens in tobacco can result in genetic alterations in the epithelial cells lining the oral mucosa. Over time, these genetic changes can accumulate and lead to genomic mutation, which results in formation of precancerous lesions, and leading to invasive oral carcinoma.[22] Additionally, tobacco use can trigger cellular proliferation by activating the EGFR receptor and related signaling pathways. This process induces cyclin D1 activation, which can lead to an increased rate of cellular proliferation and a higher likelihood of mutations occurring. Consequently, the cell may become more vulnerable to permanent genetic alterations, which can ultimately result in genomic instability and the development of invasive carcinoma. Therefore, tobacco consumption has multiple pathways to contribute to the formation of oral carcinoma.[25]

Many cancer epidemiology reports have shown that the median age at the time of diagnosis for oral cancer is 51 years old. Therefore, it is not surprising that individuals between the ages of 40 to 60 were the most likely to develop oral cancer in this study, as 50.5% of patients comes from this age group. Further, 25.62% of cancer patients come from age

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group 31-40 indicating the high tobacco consumption in young population. As a result, it may be logical to consider oral cancer screening for individuals over the age of 30 who have a higher risk of developing the disease.

Ko et al. conducted a case-control investigation that demonstrated a 123-fold increase in the incidence of oral cancer in individuals who chewed betel quid, consumed alcohol and smoked.[26,30] However, case-control studies are subject to selection bias. It is noteworthy that in this study, individuals who solely consumed alcohol did not exhibit an increased risk of developing oral cancer. One explanation for this finding may be that quantitative data on alcohol consumption was not collected. Moreover, the effects of various types of alcoholic beverages consumption on the development of oral carcinoma may vary. Therefore, it is essential to consider various factors, such as the frequency and quantity of alcoholic beverage use and the type of alcoholic beverage consumed, when studying the association between alcohol use and the development of oral carcinoma.[57]

Chaudhari Shantanu et al, shows that due to the social and cultural practices, the prevalence of addictions was found more in male compared to female 40. This is in accordance to present study in which 70.7% patients were male and 21 % were female. Study of Mahapatra et al, showed that -the respondents who consumed chewing tobacco were 6.0 times more likely to get oral cancer when compared to people who did not consume chewing tobacco.[31] The findings are similar to present study in which tobacco consumption was found to be major risk factor (i.e in 70.7% patients) for oral cancer. Further, Leopoldo Jose et al, shows that the independent effect of drinking substantially decreased and was no longer associated with oral and oropharyngeal cancer accounting for the smoking-drinking interaction term which is in accordance to present study.[1] The study of Johnson et al, showed that taken together, the effects of tobacco use, heavy alcohol consumption, and poor diet probably explain over 90 percent of cases of head and neck cancer which is consistent with present study.[34]

Previous studies have demonstrated that the combined effects of smoking and alcohol consumption lead to a high risk of oral cancer development. An alternative hypothesis proposes that alcohol plays a role in transporting carcinogens across cellular membranes. It is also known that alcohol consumption enhances liver metabolizing activity in both humans and animals, which can activate carcinogenic substances. Furthermore, alcohol may affect the intracellular metabolism of epithelial cells in the target area, making the oral mucosa more vulnerable to carcinogens from smoking and tobacco use.[6,58]

This study has several limitations that must be taken into considerations when interpreting the results. Firstly, the external validity of the findings may be constrained as the study was conducted in a single institution and only included individuals who visited the hospital seeking medical attention for oral problems. Secondly, the study did not collect precise information on the quantity of smoking, alcohol, and tobacco consumed, which restricts the ability to fully evaluate the dose-response relationship between these risk factors and oral cancer.

CONCLUSION

In this study, which followed a cohort of participants over time, we observed a significant association between tobacco use, smoking and alcohol consumption with the development of oral cancer. Our findings suggest that these three risk factors have a synergistic effect, with patients who have all three habits having a substantially higher risk of developing oral cavity cancer compared to those who do not engage in any of these habits in male population. Based on these results, we recommend that individuals aged 30 years and older, who regularly smoke cigarettes, consume alcohol, and chew tobacco should undergo regular oral mucosa screening to detect potential oral cancer as early as possible. It is important to note that early detection is crucial for successful treatment and better outcomes in patients with oral cancer.

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