Original Article

Demographic and Behavioral Risk Factors for Oral Cancer among Florida Residents

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ABSTRACT

Objectives: Almost 29,000 new cases and approximately 7,500 deaths are directly attributable to oral cancer in the United States. Understanding the impact of specific behavioral and demographic characteristics on oral cancer is crucial to being able to promote early diagnoses through oral cancer screening. This study hypothesized that selected factors would be predictive of the incidence of oral cancer in Florida's population. **Materials and Methods:** Approximately 74,000 cases from the Florida Cancer Data System (FCDS) were included in the study. Demographic and risk factors evaluated included sex, age, marital status, ethnicity, race, primary insurance payer, birthplace, cigarette use, smokeless tobacco use, cancer behavior, and other tobacco use. Logistic regression analysis was used to assess the association of 11 risk factors and oral cancer in Florida. **Results:** Males, Blacks, Hispanics, married individuals, and current smokers were significantly more likely to be diagnosed with oral cancer compared to their counterparts. **Conclusion:** Florida's health providers need to be aware of the risk factors for oral cancer, look for early signs of oral cancer and recommend routine screenings in patients with history of known risk factors. Including additional reported elements such as human papillomavirus (HPV) history, sunlight exposure, vaping and use of e-cigarettes, and alcohol consumption (by amount) in the cancer registry would be greatly beneficial.

KEYWORDS: *Demographic and risk factors, epidemiology, incidence rates, oral cancer screening*

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INTRODUCTION

Cancer is a significant cause of mortality around the world, with over six million deaths annually.[1] Although oral cancer is often sidelined in comparison to other cancers of prominence, it remains a problem of public health significance throughout the world. Indeed, head and neck cancer diagnoses account for almost 600,000 cases across the globe.[2] The US share of that figure was 53,000 cases in 2019 with the majority of the cancers involving the oral cavity and pharynx. Almost 11,000 deaths in 2019 were directly attributable to oral cancer.[3] Of all the forms of oral cancer, squamous cell carcinoma (SCC) is the most common form of oral cancer with a grim 5-year survival rate of only 50%.[4-6]

Oral cancer does not present evenly across populations. As with other cancers, increasing age, gender, and socioeconomic status are common risk factors for the disease.[7-9] Smoking and smokeless tobacco products have been significantly associated with SCC due to the prolonged contact between oral mucosa and the carcinogenic nitrosamines found in the products.[10-12] An additional risk factor for oral cancer is the chewing of betel quid (derived from the areca nut), which is primarily used in southern Asia. This product contains

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genotoxic agents and carcinogens and has become a health issue in the United States because of immigrant settlements.[13,14]

A more recently studied risk factor for oral cancer is human papillomavirus (HPV). This virus "not only increase[s] the risk of developing oral cancer, but may also contribute to its progression," and is related to the rapidly increasing incidence of oropharyngeal squamous cell carcinoma (OPSCC) in the United States.[15] Other studies have assessed the correlation of viral factors, such as HSV-1, HSV-2, CMV, EBV, and HHV-8, and oral and laryngeal cancer; however, so far there is no conclusive evidence of this relationship.[16,17] Ultraviolet (UV) light, especially UVB from sunlight exposure has long been known to cause lip cancer along the vermillion border.[7] Geographic distribution also plays a role in oral cancer incidence as it has been observed that the greatest rates occur in the southeastern and northeastern United States. In fact, Florida has the ninth highest incidence (13.2 cases per 100,000) in the country of all states and the District of Columbia.[18]

Changes in the salivary microbiota composition have also been associated with an increased risk for oral leukoplakia, oral squamous cell carcinoma, and other cancers such as pancreatic cancer.[19,20] In a study conducted by Mohammed *et al.*,[21] an association was noted between oral bacteria citing, particularly *Porphyromonas gingivalis*, and systemic cancers. Additional factors such as periodontal disease, grossly inadequate oral hygiene, a poor diet that is low in fresh fruits and vegetables, marijuana use, and recurrent fungal infections "are linked statistically with [oral] cancer but the mechanisms involved are largely unknown."[4,22]

Even with similar risk factors, mortality rates between racial groups are not equivalent.[23] Studies have shown that African American mortality rates (12.4 of 100,000) from oral cancer are nearly a third higher than in whites (9.6 of 100,000).[4] In addition, oral cancer has been found to be "two to three times more prevalent … in most ethnic groups."[7] As has been previously mentioned, many migrant population studies have shown increased number of oral cancer, especially in those traveling from southeast Asia.[24]

Materials and Methods

Data source and study sample

The data for this study were provided by the Florida Cancer Data System (FCDS). The FCDS is the "single largest population-based, cancer incidence registry in the nation . . . as over 150,000 cases are collected from patient medical records" each year.[24] Every outpatient facility and hospital in the state is required to submit a report for all patients being treated for a cancer diagnosis. Currently, the database "collects new cancer cases from 248 hospitals, 246 freestanding ambulatory surgical centers, 100 radiation therapy centers, 500 pathology laboratories, and a number of specialty physician offices, and 96% of all records in the FCDS database are histologically confirmed." The cases are submitted by the FCDS Internet Data Entry and Abstracting module (IDEA), and the reports are then checked for accuracy. The de-identified FCDS registry data for this study totaled nearly 3 million patients compiled over the last 30 years.

Variables and behavioral factors

For this study, we used FCDS Primary Site codes 0110, which encompassed all malignant tumors of the lip, tongue, salivary glands, floor of mouth, gingiva, nasopharynx, tonsils, oropharynx, hypopharynx, buccal cavity, and pharynx. Dependent variables included marital status at the time of diagnosis, sex, race, ethnicity, birth country, age, cigarette use, smokeless tobacco use, and any other form of tobacco smoking, primary insurance method at the time of diagnosis, and cancer behavior.[25]

Marital status was designated as "married" if the subject had a registered or unregistered partner, including a common law spouse. Otherwise, the participant was classified as "unmarried" if they were single, divorced, separated, or widowed. Sex was coded as dichotomous (male or female). The FCDS characterizes race as "white," "black," and "other"; this labeling structure was maintained. The label of birthplace only differentiated between from the United States and its associated territories or from any other nation. For cigarette, smokeless tobacco, or other tobacco use, the variables used a "current user," "former user," or "never" designation and did not give an indication on frequency or amount of tobacco used. Insurance was divided into five categories—no insurance, Medicaid-based insurance, Medicare-based insurance, government insurance (Tricare, Veterans Administration, Indian Health Service, and United States Public Health Service), and private insurance (Health Maintenance Organization, Preferred Provider Organization, fee-for-service, and managed care). Cancer behavior was demarcated as *in situ* or invasive based on diagnosis. Age was broken into several groups: 0–19, 20–34, 35–54, 55–64, and 65 and over years. These age-group categories were chosen based on the Kaiser Family Foundation (KFF) population distribution by age estimates for 2018.[26] All the dependent variables

account for when the patient was initially diagnosed with oral cancer.

Statistical analysis

Data were analyzed using International Business Machines Corporation (IBM, Armonk, New York, USA) Statistical Package for the Social Sciences (SPSS) statistics software (version 25.0). Descriptive statistics were calculated to summarize the demographic characteristics of the study population. Logistic regression analysis was conducted to determine whether marital status at the time of diagnosis, sex, race, ethnicity, birth country, age, cigarette use, smokeless tobacco use, and any other form of tobacco smoking, primary insurance method at the time of diagnosis, and cancer behavior were predictors of oral cancer. All significance levels were set at $\alpha = 0.05$. This study received approval from the University of West Florida (UWF) Institutional Review Board (IRB) (Number 2018–076).

Results

The analyzed sample in this study was made up of a total of 2,985,025 Florida residents from the FCDS database. Those who had been reported to the registry with a diagnosis of oral cancer made up a small fraction (2.6%) of the total registrants [Table 1]. The reported cases of oral cancer were more than two and a half times as likely to be male than female. The cases were also overwhelmingly married, non-Hispanic whites. More than three-fourths of the oral cancer cases were among individuals 55 years and older. With this information, it is of little surprise that the greatest number of reported cases of oral cancer had Medicare, a federal plan primarily for those over the age of 65 years, as their principal insurer. Almost 76% of those with oral cancer were either former or current smokers. As it has been shown in the literature, there is a clear dose–response relationship between the number of cigarettes per day and the number of years of exposure, as well as for a cumulative smoking exposure measured in pack-years, but this information was not provided in the cancer registry.[27]

The data are less striking for other tobacco products, including cigars and smokeless tobacco, as the response rates of the cases were quite low. Finally, cases of oral cancer were exceptionally likely (97.9%) to be staged as invasive at the time of their diagnosis.

With the purpose of assessing the relationship between demographic and behavioral risk factors and oral cancer, we used logistic regression analysis [Table 2]. The results of this analysis show that males were twice more likely to be diagnosed with oral cancer compared to females. Blacks were more likely to have been diagnosed with oral cancer than whites and other races ($P = 0.002$). Likewise, people of Hispanic origin were more likely to have been diagnosed with oral cancer than non-Hispanics ($P < 0.001$). In the realm of marital status, married individuals were 25% more likely to be

Table 1: Descriptive characteristics of individuals diagnosed with oral cancer

	Frequency	Percent
Sex (n = 76,868)		
Male	52,973	68.9
Female	23,861	31.1
Race (n = 73,287)		
White	66,488	90.7
Black	5,969	8.1
Other	830	1.1
Ethnicity (n = 73,078)		
Hispanic	6,297	8.6
Not Hispanic	66,781	91.4
Marital status (n = 70,964)		
Single	40,135	56.6
Married	30,829	43.4
Primary insurance (n = 50,717)		
None	3,212	6.3
Medicaid	3,754	7.4
Medicare	22,938	45.2
Government	1,815	3.6
Private	18,998	37.5
Age (years) (n = 76,864)		
0–19	290	0.4
20–34	1,167	1.5
35–54	16,913	22.0
55–64	20,692	26.9
65+	37,802	49.2
Birthplace (n = 27,582)		
United States	23,139	83.9
Other countries	4,443	16.1
Cigarette use (n = 58,652)		
Never used	14,293	24.4
Former use	21,010	35.8
Current use	23,349	39.8
Smokeless tobacco use (n = 11,760)		
Never used	10,899	92.7
Former use	288	2.4
Current use	573	4.9
Other tobacco smoke use (n = 12,625)		
Never used	10,713	84.9
Former use	388	3.1
Current use	1,524	12.1
Cancer behavior (n = 73,916)		
In situ	1,532	2.1
Invasive	72,384	97.9

Table 2: Logistic regression analysis of behavioral and demographic factors in those with oral cancer

Parameter	B	SE	Wald	OR	95% Confidence interval for OR		Sig.
					Lower	Upper	
Sex							
Female	Reference			1			
Male	0.757	0.008	9211.295	2.13	2.089	2.164	0.000
Race							
White	Reference			1			
Black	0.042	0.013	9.735	1.065	0.934	0.985	0.002
Other	0.063	0.034	3.319	1.065	0.995	1.139	0.068
Ethnicity							
Not Hispanic	Reference			1			
Hispanic	0.086	0.013	43.317	1.090	1.062	1.118	0.000
Marital status							
Single	Reference			1			
Married	0.225	0.032	50.250	1.253	1.177	1.333	0.000
Primary insurance							
None	Reference			1			
Private	0.192	0.090	4.548	1.212	1.016	1.446	0.033
Medicaid	0.308	0.074	17.532	1.361	1.178	1.571	0.000
Medicare	0.242	0.086	7.834	1.273	1.075	1.508	0.005
Government	0.447	0.073	37.304	1.563	1.354	1.804	0.000
Age (years)							
0–19	Reference			1			
20–34	0.173	0.066	6.870	1.189	1.045	1.354	0.009
35–54	1.034	0.060	300.479	2.812	2.502	3.160	0.000
55–64	0.995	0.060	279.081	2.704	2.704	3.039	0.000
65+	0.416	0.059	49.139	1.516	1.516	1.703	0.000
Birthplace							
United States	Reference			1			
Other countries	-0.066	0.054	1.518	0.936	0.842	1.040	0.218
Cigarette use							
Never	Reference			1			
Current	0.422	0.037	132.392	1.525	1.419	1.638	0.000
Former	-0.211	0.040	27.036	0.810	0.748	0.877	0.000
Smokeless tobacco use							
Never	Reference			1			
Current	0.606	0.126	23.152	1.834	1.432	2.347	0.000
Former	0.268	0.185	2.101	1.307	0.910	1.878	0.147
Other tobacco use							
Never	Reference			1			
Current	0.047	0.112	0.176	1.048	0.841	1.307	0.675
Former	-0.273	0.148	3.409	0.761	0.570	1.017	0.065
Cancer behavior							
In situ	Reference			1			
Invasive	1.148	0.104	122.669	3.152	2.572	3.862	0.000
Constant	3.000	0.159	357.982	20.094			0.000

OR = odds ratio, SE = standard error

diagnosed with oral cancer than those who were single ($P < 0.001$). With the category of primary insurance, there were five options, and no insurance was chosen as the reference. All comparisons were significant ($P < 0.05$), and had an increased likelihood of oral cancer over the reference group. The most substantial odds ratio (OR) was with government insurance (OR = 1.56), followed by Medicaid (OR = 1.36), then Medicare (OR = 1.27), and finally private insurance (OR = 1.21). This study demarcated age bands and the 0–19 years age-group was the reference group. All age brackets were significant ($P < 0.05$), and the largest OR was with the 35–54 years age-group set (OR = 2.812). The 55–64 years age-group held an OR of 2.7, whereas

the eldest group (65 years and older) had an OR of 1.51. In terms of country of origin, those born outside the United States were 6% less likely to get oral cancer (OR = 0.93), but this result was not statistically significant ($P = 0.218$). Cancer behavior held the largest OR of the study for the option of invasive diagnosis (OR = 3.15; $P < 0.001$). This was notable as this revealed that those with an invasive cancer identification were three times more likely to have oral cancer than those with the less aggressive *in situ* diagnosis. For the tobacco-based behavioral categories, cigarette use had the strongest statistical evidence ($P < 0.001$). For each of the three types, those who had never used that form of tobacco were the reference groups. The OR of current cigarette smokers was 1.52, making them 52% more likely to have oral cancer than never-smokers, whereas former smokers were 19% less likely to have that same diagnosis than never-smokers. For smokeless tobacco usage, only the comparison between never and current smokers was significant ($P < 0.001$). Current smokers were 83% more likely to have oral cancer than their never-smoking counterparts (OR = 1.83). Other forms of tobacco use held no statistically significant relationships.

Discussion

This investigation is notable as it represents, as far as we know, the first large-scale analysis of oral cancer in Florida with regard to individually associated demographic and behavioral risk factors. The large sample size used in this research includes all new cases of oral cancer that were diagnosed and reported within the state of Florida from 1981 to 2016. Other select research has been done in this area, but primarily to differentiate between oral and pharyngeal cancers with respect to their associations with race and age.[28] This new study is unique in its broad analysis of a multitude of factors relating to the development of oral cancer at large.

The findings of this study showed that certain factors are predictively associated with oral cancer. Oral cancer was more common in men than women, but that may be due to the different behavioral characteristics displayed regarding alcohol consumption and tobacco usage by men. Our results found that blacks were more prone to have oral cancer than their white counterparts. As smoking has declined among the white non-Hispanic population in the United States, "tobacco companies have targeted both African Americans and Hispanics with intensive merchandising, which includes billboards, advertising and media oriented to these communities, and sponsorship of civic groups and athletic, cultural, and entertainment events."[29]

Married persons were at an increased risk to have oral cancer, this is probably due to singles frequently being younger, have delayed diagnosis, or not being at the age when oral cancer is typically diagnosed. All age brackets were significant ($P < 0.05$). The literature has shown that people older than 45 years are at an increased risk for oral cancer, although this type of cancer can develop at any age. An interesting point was that those on government insurance such as Tricare were at the highest risk of having oral cancer. The probable causes are that many in the military use tobacco (especially chewing tobacco) at higher rates than the general population and have mandatory annual dental evaluations.[30] A large difference was expected between those born in the United States and other nations, but this was not seen. The base data for this factor were lacking so its representativeness was deficient. In the category of smokeless tobacco and cigarette usage, current users were at significantly greater risk of oral cancer. Unexpectedly, past users had a lower risk than those who had never used the products.

This study did endure several limitations. Although three-fourths of those with oral cancer were identified as either former or current smokers, there is no information in the cancer registry related to how many cigarettes the current smokers smoked within the calendar year before the diagnosis date or when the former smokers discontinued the habit before the diagnoses date. The literature shows that the risk of oral and pharyngeal cancer and oral leukoplakia in general increases with an increasing dose–response measured by the number of cigarettes per day and the number of years of exposure and declines with the duration of smoking cessation.[26,31]

We were also not able to quantify the combine effects of tobacco smoking, smokeless tobacco use and other forms of tobacco use with oral cancer. Studies have shown that when combined these risk factors with alcohol consumption, the risk increases considerable for head and neck cancer.[31]

No cancer recurrence data were provided in the cancer registry. In fact, as far as we know, there are no publicly available cancer registry data that provide cancer recurrence information. Determining the risk of cancer recurrence after primary treatment is critical to track and evaluate the evolving burden of cancer in the population.

Another limitation was that some of the variables did not have high response rates. Ideal response rates are above 90% but several categories such as birth country, primary type of insurance, and smokeless tobacco use did not meet this desired goal.

Further research is warranted and needed. Oral cancer has shown itself to present differently in diverse populations. Specifically, with many individuals continuing to participate in negative behaviors and actions that increase their risk for this deadly disease, a better understanding of the joint effect of the risk factors is needed. Further research is also needed to assess the link between oral microflora and oral cancer and the use of oral microbiota for remedial purposes. Finally, finding and examining additional reported elements such as HPV history, sunlight exposure, the effects of vaping and use of e-cigarettes, and alcohol consumption (by amount) would be greatly beneficial. This study sought to encourage public health professionals and health-care providers of all categories to further understand risk factors so that they can target oral cancer screenings and information distribution.

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Conflicts of interest

There are no conflicts of interest.

Author contributions

All the authors were involved in the analysis, interpretation of the data, and the development of the manuscript. All the authors reviewed and approved the final version of the manuscript and the primary investigator signed the final approval of the version to be published. All of the authors are accountable for all aspects of the work and are responsible for the accuracy and integrity of the work.

Ethical policy and institutional review board statement

This study received approval from the University of West Florida (UWF) Institutional Review Board (IRB) (Number 2018–076).

Patient declaration of consent

We conducted secondary analysis of a dataset that contained cases reported to the Florida Cancer Registry by Florida health care providers; therefore, no patient declaration consent was gathered.

Data availability

The dataset used in this study is available from the Florida Cancer Data System (FCDS), http://www.floridahealth.gov/diseases-and-conditions/cancer/cancer-registry/index.html.

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