A case-control study of evaluating oral squamous cell carcinoma (scc) risk factors in the Iranian population

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ABSTRACT

Introduction: Oral Squamous Cell Carcinoma is the 6th most prevalent cancer worldwide. The global increase in frequency and mortality of oral SCC has been shown. There are few studies about the risk factors for oral SCC in Iran. This study is based on finding a possible relationship between oral SCC and some lifestyle factors in the Iranian population.

Materials and Methods: This case-control study was conducted at the Iran Cancer Institute in Tehran. The controls were matched to the cases by age and gender and socio-economic status. A number of 204 individuals (102 cases and 102 controls) were interviewed by using a structured questionnaire to obtain data regarding oral hygiene, dietary factors, smoking habits, alcohol consumption and lifestyle risk factors for oral squamous cell carcinoma. Results were analyzed by chi-square and Fisher exact test. P values less than 0.05 were considered significant.

Results: The mean age of cases at diagnosis was 60.03 years and 52.9% were male. The analysis showed that poor oral hygiene, low intake of fruits and vegetables (P<0.001), low intake of dairy (P=0.029), alcohol consumption (P=0.015), cigarette smoking (P=0.002) in years and pack per year of smoking (P<0.001) are independent risk factors for oral SCC.

Conclusion: The study provided strong evidence that poor oral hygiene, poor dietary factors, smoking habits and alcohol consumption play an etiological role for oral SCC in the Iranian population.

Keywords: Risk factors; Oral squamous cell carcinoma.

Introduction

Nowadays one of the most common causes of morbidity and mortality is malignancy and annually more new cancer cases and new cancer deaths occur [1]. Oral cancer (OC) ranks sixth with approximately 274,300 new cases and 127,500 deaths occurring annually among all the cancer types in the world. Two-thirds of

recently diagnosed individuals are in developing countries while the majority of them are more than 40 years old at the time of diagnosis. This cancer is more prevalent in men [2,3]. but recently oral cancer incidence has been declined among males, whereas there has been a sharp rise among females [4]. Younger cases exhibit some sort of different high-risk behaviors related to sexual habits in comparison to older patients [5]. Only a few percent of diagnoses occur at the early stage of disease. In later stages, the treatment costs are much higher and time-consuming, more morbidity and less than a 50% five-year survival rate with optimal care is suspected [6].

The most prevalent malignant neoplasm in the oral cavity is squamous cell carcinoma (SCC). This is also the most common malignancy of the oral cavity in the Iranian Population [7]. The etiology of oral SCC is multifactorial. It is associated with tobacco use, betel quid chewing, alcohol use and low intake of fruits and vegetables [8]. The synergistic effect of these factors has been shown to increase the carcinogenic potency of tobacco and alcohol consumption [9,10]. The impact of poor oral hygiene and dental health is controversial but they have been proposed as risk factors for SCC in some studies [11,12]. Chronic infections in the mouth may also play a role in the occurrence of cancer [13]. Strong association has been shown between HPV infection and pharyngeal cancer pathogenesis [14]. Approximately a quarter of all pharyngeal squamous cell carcinomas are positive for HPV [15]. There is a scarcity of studies related to risk factors for oral SCC in the Iranian population. Thus this study has been designed to evaluate the risk factors in this population.

Materials and Methods

This study is a matched retrospective case–control study conducted at the cancer institute of Imam Khomeini Hospital in Tehran. A total number of 102 Patients diagnosed with oral Squamous Cell Carcinoma with the age range of 16 to 89 years receiving the treatment between 2018 and 2019 were included in the study. Cases were only included if diagnosed (with pathological confirmation) with a squamous cell carcinoma (SCC) of the anterior two-thirds of tongue, mouth floor, lip, buccal mucosa, gingiva or palate. (SC-C06). Patients were excluded with cancers of the salivary glands, pharynx or any other malignancy. 102 people with matched age (±three years), gender and socio-economic status were selected as controls and they were chosen from the general population who came to visit their relative patients at the hospital in any other department except the cancer institute during the study period. Control cases with any history of malignancy were excluded. Case and control samples were informed orally and manually about the study and interviewed by a single investigator using a structured questionnaire. The questionnaire was validated by using expert opinion [16,17]. The questionnaire included demographic information such as age, gender, occupation, city of residency, date and site of diagnosis (according to the patient's medical record in Iran Cancer Institute), and history of cancer in first-degree relatives. (Including father, mother, sister, brother and children). The second part of the questionnaire included questions about oral hygiene practices (such as wearing denture, interval between dental visits, use of toothbrush and toothpaste or dental floss and duration and frequency of brushing). The third part of the questionnaire contained questions about the risk factors related to cigarettes, drugs and alcohol consumption detailed by type, frequency, duration and start time of the habits. Finally the last part of the questionnaire including questions about some food intake habits [18,19]. Few data has been cited because they were beyond the scope of this paper. The recorded data from the 204 cases and controls were subjected to statistical analysis [20] using Chi-square [21] and Fisher exact test and adjusted odds ratio (ORs). The 95% confidence intervals (CI) were calculated to estimate the suspected risk factors for oral SCC by using multivariate logistic regression analysis [9,22]. The Statistical Package for Social Sciences (SPSS) version 21.0 was used for the statistical analysis and the significance level was set at $P<0.05$ [23].

Results

A total of 204 cases/controls with an age range of 16-89 years were enrolled in this study, 102 oral SCC patients (54 males and 48 females) and 102 non-oral cancer controls (54 males and 48 females). The median age of cases was 60.03 years with a standard deviation of 16.675 years. The median age of the control group was 59.62 years with a standard deviation of 16.242 years. The frequency of cancer sites in oral SCC patients (n=102 patients) were: 43 (42.2%) tongue, 20 (19.6%) buccal mucosa, 18 (17.6%) lips, 14 (13.7%) floor of mouth, 3 (2.9%) gingiva and 1 (1%) palate. 3 others (3%) were involved by two other areas. First-degree relatives (parents, sisters, brothers and children) of 34.3% of the cases and 27% of the controls had a history of any other malignancy, so, a significant relationship between a history of cancer in first-degree relatives and the incidence of oral SCC was not found

(p=0.223).

Analysis of exposure to risk factors

Oral hygiene

Among the 102 cases, 91.9% of them did not have regular dental checkups before the diagnosis. 8.8% of those had dental checkups regularly as every 6 to 18 months and none of them noted dental checks less than every 6 months. In the control group result were 81.4%, 15.7% and 2.9% respectively. According to statistical analysis, a significant relationship was seen in conjunction with regular dental visits (p value=0.037). In addition to brushing 58.8% of controls and 32.4% of cases before diagnosis used to brush their teeth at least once a day. The frequency of daily tooth brushing and its duration are shown in Table 1.

In addition to brushing, 1% of the total cases also used dental floss at least once a day, but in the control group, 17% used dental floss. Also, 49% of cases and 36.2% of controls reported wearing a removable complete or partial denture. Prolonged use, and long-duration (≥5 years) of dentures were not associated with an increased risk of SCC occurrence. The analysis revealed that the odds of SCC related to denture injury was 3.72 (95% CI: 1.649, 8.390; P=0.001) higher in comparison with the absence of such a history. Actually, 8.8% of total cases and 26.5% of controls had a history of an injury with the denture. Statistical analysis of oral hygiene is demonstrated in Table 2.

Food intake

According to the analysis, it seems that people in the control group received more fruits, vegetables (P<0.001) and more dairy (p=0.029) compared with the cases. There were no significant differences between cases and controls in intake of meat (p=0.23),

black tea (p=0.35) or coffee (p=0.55) (Table 3).

Smoking and alcohol consumption

In this study 49% of cases and 28% of controls recorded no smoking history, 7.8% of cases smoked less than 5 cigarettes per day (low amount), 8.8% smoked 5 to 15 cigarettes per day (moderate amounts), 24.5% smoked 15 to 30 cigarettes per day (heavy amounts) and 6.9% smoked more than 30 cigarettes per day (very heavy amounts) compared to controls who generally smoked less (14.7% of controls: low amount, 8.8: moderate amounts, 3.9%: heavy amounts and 0.0%: very heavy amounts). So an increase in the amount of smoked cigarettes may lead to an increase in SCC prevalence (p<0.001). Regarding the age cases started smoking; 13.7% of cases and 4.9% of controls started smoking at less than 20 years old, 33.3% of cases and 20.6% of controls started at 20 to 40 years old and no case and 2.0% of controls started at more than 40 years old. It shows that smoking initiation at young age is also a risk factor (p=0.012). Duration of smoking cigarettes, smoking hookah, alcohol use and opioids consumption has been shown in Table 4. The frequency of hookah smoking and drinking alcohol is shown in Table 5. A statistically significant difference was noted between duration and amount of smoking cigarettes in this study population (P=0.002). An increased risk of SCC was associated with an increased duration of any opioid consumption (P=0.006) and an increased amount of alcohol consumption and increased duration of consumption (p=0.01). A dose response was observed for both frequencies. However our data showed no significant effect of duration and frequency of hookah use on elevated risk of SCC (p=0.06) (Table 6).

Table 1. The number of tooth brushing per day and Duration of tooth brushing.

	Without brushing	Once a day	Twice a day	3 or more times	Without brushing	<2 min	2 to 5 min	>5 min
Control	43	43	12	4	42	24	34	2
	42.2%	42.2%	11.8%	3.9%	41.2%	23.5%	33.3%	20%
Case	69	30	3	0	69	19	14	0
	67.6%	29.4%	2.9%	0.0%	67.6%	18.6%	13.7%	0.0%

Table 2. Odds ratios (OR) and corresponding 95% confidence intervals (CI) for oral cancer in 102 cases and 102 controls.

	OR	95%CI	P value
Brushing	0.334	0.188,0.593	<0.001
Regular brushing	0.369	0.195,0.700	0.002
Using toothpaste	0.320	0.180,0.568	<0.001
Flossing	0.049	0.064,0.379	<0.003
Wearing denture	1.68	0.964,2.957	0.066
History of injury	3.72	1.649,8.390	0.001

Table 3. Intake of food.

			No intake	1 unit in week to 1 unit in day	1 or 2 units per day	3 or 4 units per day	5 or more units per day
Fruits and vegetables	Control	Count	3	3	54	38	4
		%	2.9%	2.9%	52.9%	37.3%	3.9%
	Case	Count	11	30	37	22	2
		%	10.8%	29.4%	36.3%	21.6%	2.0%
Dairy	Control	Count	9	11	64	17	1
		%	8.8%	10.8%	62.7%	16.7%	1.0%
	Case	Count	6	25	63	8	0
		%	5.9%	24.5%	61.8%	7.8%	0.0%
Meat	Control	Count	16	52	32	2	0
		%	15.7%	51.0%	31.4%	2.0%	0.0%
	Case	Count	9	55	33	5	0
		%	8.8%	53.9%	32.4%	4.9%	0.0%
Black tee	Control	Count	4	7	17	42	32
		%	3.9%	6.9%	16.7%	41.2%	31.4%
	Case	Count	2	1	26	33	40
		%	2.0%	1.0%	25.5%	32.4%	39.2%
Coffee	Control	Count	65	6	1	0	0
		%	93.1%	5.9%	1.0%	0.0%	0.0%
	Case	Count	97	4	0	1	0
		%	95.1%	3.9%	0.0%	1.0%	0.0%

Table 4. Duration of smoking cigarettes, smoking hookah, alcohol drinking and opioids consumption in study population.

			No usage	Less than one year	1 to 10 years	10 to 20 years	20 to 30 years	More than 30 years
smoking cigarettes	Control	Count	74	1	6	11	6	4
		%	72.5%	1.0%	5.9%	10.8%	5.9%	3.9%
	Case	Count	53	2	7	8	14	18
		%	52.0%	2.0%	6.9%	7.8%	13.7%	17.6%
smoking hookah	Control	Count	93	0	5	4	0	0
		%	91.2%	0.0%	4.9%	3.9%	0.0%	0.0%
	Case	Count	85	1	9	6	1	0
		%	83.3%	1.0%	8.8%	5.9%	1.0%	0.0%
Alcohol drinking	Control	Count	96	0	5	0	0	1
		%	94.1%	0.0%	4.9%	0.0%	0.0%	1.0%
	Case	Count	85	1	8	4	4	0
		%	83.3%	1.0%	7.8%	3.9%	3.9%	0.0%
Black tee	Control	Count	100	0	2	0	0	0
		%	98.0%	0.0%	2.0%	0.0%	0.0%	0.0%
	Case	Count	90	3	2	4	1	2
		%	88.2%	2.9%	2.0%	3.9%	1.0%	2.0%

Table 5. Frequency of hookah smoking and alcohol drinking.

			No intake	1 unit in week to 1 unit in day	1 or 2 units per day
Hookah Smoking	Control	Count	93	4	5
		%	91.2%	3.9%	4.9%
	Case	Count	85	15	2
		%	83.3%	14.7%	2.0%
Alcohol Drinking	Control	Count	97	3	2
		%	95.1%	2.9%	2.0%
	Case	Count	85	17	0
		%	83.3%	16.7%	0.0%

Table 6. Odds ratios (OR) and corresponding 95% confidence intervals (CI) for oral cancer in 102 cases and 102 controls.

	OR	95%CI	P value
Cigarette smoking	2.443	1.363,4.377	0.002
Hookah smoking	2.214	0.943,5.195	0.06
Alcohol consumption	3.200	1.206,8.487	0.01
Opioids	6.666	1.452,30.59	0.006

Discussion

Cancer is the second cause of death in developed countries and the 10th most common cause of mortality in developing countries. Oral cancer represents approximately 13% of all cancers or 30,000 new cases each year [9]. The primary aim of this case-control study was to evaluate the major risk factors for oral squamous cell carcinoma in the Iranian population. In total, 102 cases were admitted in the study from the cancer institute of Imam Khomeini Hospital, one of the biggest centers in Iran. Gender and marital status were equal between cases and controls in the study. The age range occurrence of SCC in our study population was 16 to 89 years. The main limitations of this study were ailment of 58.8% of patients so we interviewed them in association with their first degree relatives. Possible biases that could account for the current findings include lack of relative's awareness.

The most common site of OSCC occurrence was tongue and the prevalence of smoking was highest in patients with SCC of the mouth floor and lowest for cancer of the tongue. The mean age for initiation of habits was 20 to 30 years old. Our study confirmed the previous findings and showed that the amount of daily cigarettes smoked and the duration of smoking has a direct relationship with OSCC. Also, our study found a statistically increased risk of oral cancer among heavy smokers. It was also the same for opioid usage and alcohol consumption. Hookah smoking among the population was associated with an increased, but not a statistically significant, risk of OSCC. The present study suggested that indicators of dental care were worse among cases and cases might have poor general oral hygiene than control subjects, as indicated by less brushing, less dental checkups and less flossing (ORs for brushing=0.334, dental checkups=0.369, and for flossing=0.049). Findings regarding oral hygiene, however, must be interpreted with great caution. This study tends to agree with findings in Talamini et al. The study [24] which showed no adverse effect of denture use (OR=1.68, 95%CI=0.964, 2.957). It also showed a significant relationship between SCC occurrence and malignant transformation of denture-induced lesions (OR=3.72, 95%CI=1.649, 8.390). In this study, the numbers of food and food groups were investigated and an inverse association emerged for fruit and vegetable intake and an inverse one for dairy intake. Such a risk pattern is consistent with previous findings in the Garrote et al. study [25] but there were no significant differences between cases and controls in the intake of meat, black tea and coffee.

In conclusion, to the best of our knowledge, this is one of the first case-control studies to assess the risk factors of tobacco, alcohol, poor oral hygiene and diet among the Iranian population with oral SCC. While our paper reported highly elevated risks for tobacco and alcohol usage, low intake of fruits and vegetables and poor oral hygiene among the population with oral squamous cell carcinoma our results indicate that exposure to these risk factors in the Iranian population is similar to patients in other countries. However, it is questionable whether the rate of exposure to alcohol compared with other countries is significant enough to become an etiology for oral SCC or not. It may be related to Iranian religious prohibitions for alcohol consumption. However, use of alcohol is increasing not only among men but also among children, teenagers, and women.

Conflict of Interest

There is no conflict of interest to declare.

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