Original Article

An Epidemiologic study of Oral and Pharyngeal Nonsquamous Cell Malignant Tumors in Kerman province, Iran

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Abstract:

Objective: The aim of the present study was to estimate crude and age-standardized incidence rates for oral and pharyngeal nonsquamous cell malignant tumors in Kerman province over a period of 11 years.

Materials and Methods: The data used in this retrospective population-based study were extracted from the records registered in all pathology centers of Kerman province from 1991 to 2001. All confirmed cases of oral and pharyngeal nonsquamous cell malignant tumors were included in the study. The crude and age-standardized incidence rates per 1 million populations were calculated based on the 1996 census data and the population growth rate.

Results: The total number of new nonsquamous cell cancers was 61, representing 18.2% of all oral and pharyngeal cancers in Kerman province. The average annual age-adjusted incidence rate per 1,000,000 population was 3.45 for both oral and pharyngeal tumors. The temporal variations in the annual incidence of oral and pharyngeal nonsquamous cell cancers was statistically significant (p=0.015). The most common types of nonsquamous cell malignant tumors in the oral cavity and pharynx were minor salivary tumors and lymphomas, respectively. The age-adjusted incidence was 0.74 for malignant salivary gland tumors, 0.66 for malignant melanomas, 0.4 for different types of sarcomas, and 1.65 for lymphomas.

Conclusion: It can be concluded that the incidence rate and other features of nonsquamous cell malignant tumors of the oral cavity and pharynx in residents of Kerman province are similar to those reported by other investigators.

Key Words: Epidemiology; Oral cancer; Pharyngeal cancer; Oral malignant melanoma; Oral sarcoma; Minor salivary gland tumor

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INTRODUCTION

Oral cancer is one of the ten most common cancers worldwide, accounting for 274,000 new cases in 2002 [1]. It predominantly affects middle-aged and elderly individuals and is more common in males than females, but the sex ratio is growing closer to unity. The main risk factors of oral cancer are cigarette smoking and alcohol consumption [2,3]. However, recent studies have shown that diets low in fresh vegetables and fruits, exposure to viruses especially high-risk types of human papillomavirus, and genetic predisposition may also increase the risk of oral malignancies [4-7]. In spite of the fact that squamous cell carcinoma is the most common type of oral cancer

representing approximately 90 to 94 percent of malignant tumors in this site, many other types of cancers also exist in the oral cavity. These include minor salivary gland carcinomas, different types of sarcoma, lymphomas, primary oral malignant melanomas and metastatic cancers from other organs [8]. Epidemiologic studies have shown that the incidence and relative frequency of oral cancer varies in different parts of the world, probably due to a different prevalence of specific risk factors. About 75% of all oral cancers occur in developing countries, especially in Southeast Asia and the Indian subcontinent, where the oral cavity is often the first or second most common site of malignancy [9]. The incidence of oral cancer in Western countries is relatively low, although some studies have shown that its occurrence in some parts of Europe and the United States is increasing, especially among young men [10-13]. The vast majority of data on the epidemiological aspects of oral cancer comes from Western countries and relatively little is known about the incidence of these tumors in other parts of the world, especially in the Middle East. To our knowledge epidemiologic studies on malignant tumors of the oral cavity and pharynx are limited in the Iranian population. The purpose of the present investigation was to describe the incidence and relative frequency of oral and pharyngeal nonsquamous cell malignant tumors in Kerman province over a period of 11 years from 1991 to 2001.

MATERIALS AND METHODS

In this study, the term oral and pharyngeal cancer refers to malignant tumors according to International Classification of Disease for Oncology (ICD) of the lips (ICD9 140), tongue (ICD9 141), mouth (ICD9 143-145), and pharynx (i.e. oropharynx, ICD9 146; nasopharynx ICD9 147; hypopharynx, ICD9 148; unspecified sites, ICD9 149). Case definition for the current investigation is any nonsquamous cell malignant neoplasm diagnosed for the first time in a resident of Kerman province between 1991 and 2001 in one of the abovementioned sites. Major salivary gland cancers (ICD 142) were excluded from the present study. Considering that there was no comprehendsive cancer registry in Kerman province until 2002, the data used in this epidemiologic investigation were extracted directly from pathology records registered in all public and private pathology centers of Kerman during the study period. Cases that were registered twice or had incomplete information were eliminated from the study material. A description of variables including: sex, age, and histological type were recorded. Population estimates were based on the 1996 census data

Table I: Distribution of 61 nonsquamous cell malignant tumors according to age and sex in Kerman province.

Type of Lesion	Cases	Age			Sex		
		Range	Mean	Median	Male	Female	M/F ratio
Oral cavity and the lips							
Minor salivary gland tumors	13	10-72	40.2	40	6 (46.2%)	7 (53.8%)	1:1.2
Malignant melanoma	9	56-77	66.1	70	6 (66.7%)	3 (33.3%)	2:1
Different types of sarcoma	8	11-58	29.1	30	1 (12.5%)	7 (87.5%)	1:7
Lymphoma	8	1-65	29.7	23.5	6 (75%)	2 (25%)	3:1
Metastatic tumor	1	NA*	NA	NA	0	1 (100%)	NA
Total	39	1-77	41.2	44	19 (48.7%)	20 (51.3%)	1:1.05
Pharynx							
Lymphoma	20	6-85	42.8	45	14 (70%)	6 (30%)	2.3:1
Malignant melanoma	1	NA	NA	NA	0	1 (100%)	NA
Metastatic tumor	1	NA	NA	NA	0	1 (100%)	NA
Total	22	6-85	44.6	49	14 (63.6%)	8 (36.4%)	1.75:1

and population growth rate, provided by the Statistical Center of Iran. The crude and age-adjusted incidence rates for nonsquamous cell malignant tumours of the oral cavity and pharynx, standardized to the world population, were calculated and expressed per 1 million population. To assess the effect of age and sex, and to determine time variations, risk ratios were estimated using the negative binomial method. Incidence rates, risk ratios and the corresponding 95% confidence intervals were calculated. Data processing was performed using the Stata version 8.0 software.

RESULTS

Between 1991 and 2001, a total number of 334 new cases of oral and pharyngeal cancer (262 cases in the oral cavity and the lips and 72 cases in the pharynx) were diagnosed in Kerman province. Nonsquamous cell malignnant tumors accounted for 61 (18.2%) cases of which 39 (63.9%) were in the oral cavity and lips and 22 (36.1%) were in the pharynx. As far as the oral cavity and the lips are concerned, cancers of the minor salivary glands were the most common nonsquamous malignant tumors, representing 33.3% (13) of the cases followed in decreasing order by malignant melanoma (9/39, 23.1%), different types of sarcoma (8/39, 20.5%), lymphoma (8/39, 20.5%), and metastatic tumors (1/39, 2.6%). Lymphoma was the most common type of nonsquamous cell malignant tumor of the pharynx comprising 90.9% (20) of the cases. The distribution of 61 nonsquamous cell malignant tumors of the mouth and pharynx according to age and gender are shown in Tables I and II. The crude incidence rate for nonsquamous cell malignant tumors of the oral cavity and pharynx (excluding metastatic tumors) during the 11-year study period was 2.63 per one million population and the age-standardized incidence rate was 3.45 per one million population (Table III). Temporal variations in the annual incidence of oropharyngeal nonsquamous cell cancers was statistically significant (P=0.015). The estimated risk ratio for the linear effect of time (year) was 1.11 (95%CI: 1.02-1.21). This implies that on average the risk of reported nonsquamous cell malignant tumors of the oropharyngeal region increased around 11% each year during the entire study period (Fig. 1).

Other characteristics of nonsquamous cell malignnant tumors evaluated in the present study are as follows:

Cancers of the minor salivary glands: The mean age of patients with malignant tumors of the minor salivary glands was 40.2 (17.8) with a range of 10 to 72 years. The distribution of these tumors in males and females was almost equal (M/F 1:1.2). Palate was the most common location of malignant tumors of minor salivary glands in our series (8/13, 61.8%), followed by buccal and vestibular mucosa (4/13, 30.8%) and the upper lip (1/13,

Table II: Age distribution of nonsquamous cell malignant tumors (excluding metastatic tumors).

Age (yr)	MSGT			Malignant melanoma			Sarcoma			Lymphoma		
	M	F	Both (%)	M	F	Both (%)	M	F	Both (%)	M	F	Both (%)
0-9	0	0	0	0	0	0	0	0	0	6	0	6 (21.4)
10-19	2	0	2 (15.4)	0	0	0	0	3	3 (37.5)	1	0	1 (3.6)
20-29	0	0	0	0	0	0	0	0	0	3	0	3 (10.7)
30-39	1	3	4 (30.8)	0	0	0	1	2	3 (37.5)	3	0	3 (10.7)
40-49	2	3	5 (38.5)	0	0	0	0	1	1 (12.5)	1	2	3 (10.7)
50-59	0	0	0	1	0	1 (10)	0	1	1 (12.5)	3	2	5 (17.9)
60-69	0	1	1 (7.7)	2	2	4 (40)	0	0	0	1	3	4 (14.3)
70-79	1	0	1 (7.7)	3	2	5 (50)	0	0	0	1	1	2 (7.1)
80-89	0	0	0	0	0	0	0	0	0	1	0	1 (3.6)
Total	6	7	13 (100)	6	4	10 (100)	1	7	8 (100)	20	8	28 (100)

7.7%). The predominant histologic type was adenoid cystic carcinoma representing 46.2% (6) of all cases. The overall crude and age-standardized incidence rate of malignant tumors of the minor salivary glands during the 11-year study period were 0.59 and 0.74 per one million population, respectively (Table IV).

Primary oral malignant melanom: Malignant melanoma accounted for 3.4% of all oral cancers. The patients' age ranged from 56 to 77 years with a mean of 65.5 (7.0) years. Males were affected more than females and the male to female ratio was found to be 1.5:1. Malignant melanoma affected the lower lip and buccal mucosa, but the most common site was the palate (7/10, 70%). The total number of melanoma diagnosed between 1991 and 2001 in Kerman province was 187; of these, 4.8% (9/187) occurred in the oral cavity. The overall crude and age-standardized incidence rate for oral and pharyngeal malignant melanoma during the study period were 0.45 and 0.66 per one million population, respectively.

Sarcoma: The age range of patients with different types of sarcoma was between 11 and 58 years with a mean (SD) of 29.1 (15.6) years. Most of the patients with sarcoma in our series were females (M/F 1:7). Buccal and vestibular mucosa was the most common location of sarcoma in the present study population (5/8, 62.5%). The site of the lesion in three cases was not specified. The crude and age-standardized incidence rates for oral sarcoma were 0.36 and 0.4 per one million population, respectively.

Lymphoma: Lymphoma accounted for 3% of all oral cancers and 15.5% of all pharyngeal cancers. Of the 28 patients with oral and pharyngeal lymphoma, 20 (60.6%) cases were male with a male to female ratio of 2.5:1. The mean age of the patients was 39(25) years ranging from 1 to 85 years. Most lymphomas were located in the palatine tonsils (14/28, 50%). Other locations of lymphoma were the gingiva (5/28, 17.9%); pharynx, unspecified (6/14, 21.4%); palate (1/14, 3.6%); tongue (1/14, 3.6%); and upper lip (1/14, 3.6%). The crude incidence rate for oral and pharyngeal lymphoma was 1.27 per one million population and the age-standardized rate was 1.65 per million population during the entire study period.

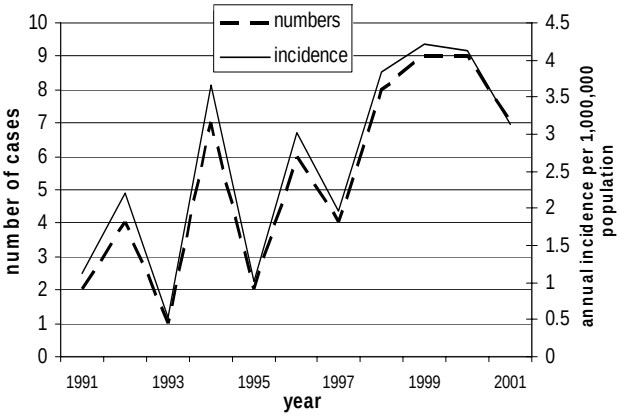

Fig. 1: Temporal variation of the annual incidence of oropharyngeal cancer

Metastatic tumor: There were two metastatic tumors in our study population. The first one was a gingival metastasis from a primary breast cancer and the second one involved palatine tonsils, and was diagnosed as metastatic papillary carcinoma.

Table III. Crude and standardized annual incidence rate of nonsquamous cell oral and pharyngeal cancers, classified by sex in one million population

	Sex	Crude incidence	Standardized	
			Incidence	95% CI
Oral	Male	1.7	2.01	1.08-2.94
	Female	1.75	2.3	1.23-3.36
	Total	1.72	2.16	1.45-2.87
Pharyngeal	Male	1.25	1.62	0.73-2.5
	Female	0.65	0.99	0.26-1.73
	Total	0.95	1.29	0.72-1.86
All	Male	2.95	3.62	2.34-4.91
	Female	2.4	3.29	1.99-4.58
	Total	2.63	3.45	2.54-4.36

DISCUSSION

The incidence of nonsquamous cell malignant tumors of the oral cavity and pharynx has not been extensively investigated in Iran. Iran is the second largest country in the Middle East with a population of nearly 70 million people. Kerman is the largest province in the country, located in the Southeast of Iran, with a population of over 2.5 million persons. The vast majority of the people living in Kerman are Muslims. The overall consumption of alcohol is very low and almost entirely limited to the urban male population. Smoking cigarette, opium, and hookah is socially acceptable and common, especially among men. During our 11-year study period, 59 cases of oropharyngeal nonsquamous cell malignant tumors (excluding metastatic tumors) were diagnosed in Kerman province. The incidence was estimated to be 3.45 per million population. A descriptive report on the epidemiology of cancer such as the present study can be criticized for validity of data. For example, people from lower socioeconomic groups and nomadic tribes who live in the Southern regions of Kerman usually do not seek medical attention leading to a number of undiagnosed cases. In addition, some cancer patients may be referred to centers or hospitals outside Kerman. In spite of this, the oropharyngeal area especially the oral cavity is very accessible for examination and tissue sampling. Therefore, malignant tumors in these regions have a good chance of being detected by both patients and clinicians even in the early stages. Furthermore, due to the dysfunction and dysfigurement caused by oropharyngeal tumors, even the most careless patients usually feel the need to seek professional help. Considering these, we believe the incidence rate of nonsquamous cell oral and pharyngeal cancers reported in the present study can be regarded as a relatively accurate figure for Kerman province.

Table IV: the crude and standardized annual incidence rate of oropharyngeal nonsquamous cell cancers, classified by sex and type in one million population.

	Sex	Crude incidence	Standardized	
			Incidence	95% CI
Salivary	Male	0.54	0.61	0.1-1.11
	Female	0.65	0.87	0.22-1.51
	Total	0.59	0.74	0.33-1.15
Melanoma	Male	0.54	0.75	1.5-13.5
	Female	0.37	0.56	0.1-11.2
	Total	0.45	0.66	2.5-10.7
Sarcoma	Male	0.09	0.11	0.0001-0.33
	Female	0.65	0.7	0.15-1.25
	Total	0.36	0.4	0.11-0.7
Lymphoma	Male	1.79	2.16	1.17-3.15
	Female	0.74	1.16	0.35-1.96
	Total	1.27	1.65	1.02-2.29
All	Male	2.95	3.62	2.34-4.91
	Female	2.4	3.29	1.99-4.58
	Total	2.63	3.45	2.54-4.36

The increased risk of non-squamous cell oral and pharyngeal cancers between 1991 and 2001 was statistically significant, although it was not considerable. This slight increase might be due to improvement in the registration of cancer and a decrease in reporting bias. However, other factors such as aging could be partially responsible for this increase.

There were 9 new cases of primary oral malignant melanomas in our study population corresponding to an incidence rate of 0.66 per million population. This figure is higher when compared with the incidence rate of 0.12 per million population for oral malignant melanoma reported from other countries [14]. In the current investigation, the age of patients with primary oral malignant melanoma ranged from 56 to 77 and this tumor was more prevalent in males than in females. The palate was the most common site of involvement. These findings are in accordance with those described by others [14-16]. Oral malignant melanomas in the present study comprised 4.8% of all melanomas which was higher compared to the 1% reported by Hicks and Flaitz [14]. The incidence of minor salivary gland tumors in the present study was 0.74 per million popula-

tion which is close to that reported by Koivunen et al [17] from Northern Finland. Adenoid cystic carcinoma was the most common malignant tumor of the minor salivary glands in our series representing 46.2% of the cases. This finding is in agreement with previous studies [18,19]. Other characteristics of the tumors of minor salivary glands including location, age and sex were also similar to those reported by Poomsawat et al [20] and Loyola et al [21]. Eight cases of oral lymphoma were identified in the current investigation accounting for 3% of all oral cancers. This is similar to the 3.5% to 4% reported from British Columbia and Jordan [22,23].

CONCLUSION

In conclusion, the incidence rate and other features of nonsquamous cell malignant tumors of the oral cavity and pharynx in Kerman province are similar to those reported by others. However, the incidence and relative frequency of oral malignant melanoma in the present study was relatively high, necessitating further attention in future studies.

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