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Original Article

Epidemiological Aspects of Oral and Pharyngeal Cancer in Kerman Province, South Eastern Iran

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Abstract

Background: Epidemiologic aspects of oral and pharyngeal cancers in Iran have not been studied adequately. We evaluated age-adjusted incidence rates by sex using pathological confirmed cases between 1991 and 2002 in Kerman Province, south eastern Iran.

Methods: The information of cases was collected actively from all of the 18 histopathology departments around the province. The standardize risks were estimated using standard world population and the risk ratio for age and sex were estimated using negative binomial model.

Results: The total number of newly diagnosed malignant oral and pharyngeal cancers was 334, represented 3.1% of all newly diagnosed cancers. The age-adjusted incidence rate for oropharyngeal cancers was 2.21 cases per 100 000 populations per year. The results suggested that those age 40 and over were 18.1 times more likely to develop oral and pharyngeal cancer than the younger group. The risk of developing oral and pharyngeal cancers was 1.75 times more common in males than females.

Conclusion: This study showed that the overall incidence of oral and pharyngeal cancers in Kerman Province was lower than that in most parts of the world. The lower incidence might be due to behavioral differences such as low consumption of alcohol, chewing tobacco, and spicy foods.

Keywords: *Oral, Pharyngeal, Cancer,* Epidemiology*, Iran*

Introduction

Oral and pharyngeal cancer is estimated to be the sixth most common malignancy worldwide; however, it has attracted relatively little attention from epidemiologists compared to many other forms of cancer (1-3). The incidence of oral cancer shows considerable geographical, cultural and ethnic variations. This variation ranges from a low incidence of 1-2% of all malignant tumors in much of Japan to over 40% in Sri Lanka and approaching 50% in India (3). Many studies have noted that the variation can be explained, in part, by the different prevalence of the main risk factors, alcohol and tobacco, in various geographic areas and in each of the sexes (4, 5). Geographical or regional variations in the prevalence of oral cancer indicate that the sociocultural lifestyles of a population play an important role in oral carcinogenesis (6).

Iran is a large country located in the Middle East and Kerman is the largest province in Iran covering 11% of the total area of this country. This province has a population of about 2.5 millions and is located in the southeast of Iran. Reviewing the literature shows few population-based data on the incidence of oropharyngeal cancers in Iran especially in Kerman Province. This report represents the first population-based study to report the status of oral and pharyngeal cancers in Kerman Province.

The purpose of this study was to estimate the annual risk of oral and pharyngeal cancers classified by age group and sex. Moreover, the temporal variations of the incidence of oropharyngeal cancer were assessed between 1991 and 2002.

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Material and Methods

The information of cases was collected actively from the archives of all of the 18 histopathology departments around Kerman Province. These departments receive nearly all pathology specimens from private and public hospitals and clinics throughout the entire province. Data collection began in the year 2003 and continued for about 2 years. The case definition was done according to WHO/ICD9; all newly proven primary malignant oral and pharyngeal tumors among Kerman residents between 21 March 1991 (Iranian New Year) and 20 March 2002 were enrolled in the analysis. The following sub-locations of the oral cavity were studied: lip, tongue, gum, floor of the mouth, other parts of the mouth, oropharynx, nasopharynx, hypopharynx and ill-defined sites (7). Malignant neoplasms of major salivary glands were not included in this study. Only cases of primary oral and pharyngeal cancers were considered in this report; no recurrent, in situ or benign lesions were included. The crude and age and sex standardized incidence rates of malignant tumors were computed classified by anatomic site and expressed per 100,000 person-years.

Using direct method, the incidences were standardized based on the standard world population (8). The age and sex standardized is a weighted average of the age-specific rates, where the weights are the proportions of persons in the corresponding age and sex groups of the WHO standard population. The WHO World Standard Population was estimated based on the average world population structure for the period 2000-2025.

The population pyramid of Kerman Province was extracted from the national census in 1996. The annual total population of Kerman between 1991 and 2001 were interpolated based on the census data and population increase rate. The relative risks for sex and age group and the temporal variation of oropharyngeal cancers were estimated using negative binomial models. By the negative binomial method, the risk ratios (RR) and their confidence intervals were estimated to compare the risk of developing oral and pharyngeal cancers in males and females, in those 40 yr old and over and in those aged less than 40. Stata version 8 was used for these analyses.

Results

Oral cavity and pharynx

The total number of new malignant oral and pharyngeal cancers for the period 1991-2002 was 334, representing 3.1% (4.7% of all males and 2.6% of all females) of all newly diagnosed cancers. Oral and pharyngeal cancer was the seventh most common cancer of the body in both sexes. The crude incidence and standardized rates of oropharyngeal were 1.50 and 2.21 cases per 100,000 population per year respectively (Table1). Using the negative binomial model, the variations in the annual incidence of pharyngeal cancers was statistically significant (P= 0.002). The estimated risk ratio for linear effect of year was 1.11 (95% CI: 1.03-1.2) between 1991 and 2001 (Fig. 1). However, the annual variations of oral cancers were not statistically significant (RR= 1.03, P= 0.09) (Fig. 1). Due to low sample size the power of test was very low to check the departure from the linear trend; however, ignoring the very low number of pharyngeal cancer in 1995, by eyeballing we may presume a linear trend. However, we do not have any explanation for dip in 1995.

Histologically the majority of oral and pharyngeal cancers (71.3%) were squamous cell carcinoma (SCC). Of SCC cases, 91,6% occurred in the oral cavity and 8.4% in the pharyngeal region. Other histological types were: nasopharyngeal carcinoma (8.4%), lymphoma (8.1%), malignant minor salivary gland tumors (3.9%), melanoma (3.0%), sarcoma (2.4%) and others (3.6%). The mean and median age of the patients, were 54.55 and 60 yr respectively (range 1 to 85 yr), 21.6% of malignant tumors occurred in less than 41 yr old and 50.9% in more than 59 yr old. The incidence rate increased with age and the highest incidence rate was in the age group 60-

69 yr (Fig. 2). Oral cancer in all age groups was much more common in males than females (Fig. 3).

The results suggested that those age 40 and over were 18.1 times more likely to develop oral and pharyngeal cancer than the younger group. The risk of developing oral and pharyngeal cancers was more common in males than females (Table 2).

Pharynx

Seventy two pharyngeal malignant tumors were diagnosed during the study period. The male: female ratio was 0.96:1. The mean age was 46.02 for men and 44.31 for women. Malignant tumors of the pharynx accounted for 0.68% of all malignancies of the body. For the whole pharynx, the incidence rate was 0.49 cases per 100,000 per year for males and 0.40 for females (Table1). Most (39%) of the malignant tumors of the pharynx were nasopharyngeal carcinoma. Squamous cell carcinoma and lymphoma accounted for 26 and 28% of cases, respectively.

Oral cavity

If malignant tumors of the pharynx were excluded, the total number of new cases of the lips and intraoral region amounted to 262 cases, representing 2.48% of all newly diagnosed malignant tumors in Kerman province (3.04.% of male and 1.80.% of female cancers). The male to female ratio was 2.1/1.The standardized incidence rate of oral cancer was 1.75 per 100,000 (Table1). The mean age for males and females was comparable (males: 56.91 and females: 57.51). About 83% of malignancies were squamous cell carcinoma.

Lip

The most frequent site of oral and pharyngeal cancers was the lip accounting for the 113 cases (33.8 %). Age adjusted incidence rate of lip cancers was 0.8 per 100,000 (Table3). The male: female ratio was 4.65:1. Lip cancer was almost 7.36 times as frequent in the lower lip as in the upper lip. The majority of lip cancers were found in the lower lip of males. The male: female ratio was 2.6:1 for the upper lip and 6.3:1 for the lower lip. Squamous cell carcinoma accounted for 95.5% of cases.

Tongue

Cancer of the tongue was next to that of the lip. The total number of primary malignant tumors diagnosed in the tongue was 51 cases (15.3%) and more than 96% of the cases were SCC. The male:female ratio was 1.04:1. The age adjusted incidence rate was 0.3 per 100,000 (Table3).

Other sites

Table 3 shows the standardized incidence rates of malignancies in different sites of the oral cavity and pharynx. After lip and tongue, other most common sites of involvement were other and unspecified parts of the mouth, nasopharynx, gum, oropharynx, hypopharynx and other and ill defined sites within the lip, oral cavity and pharynx respectively. The incidence of oral cancers of the floor of the mouth was very low.

Table 1: The crude and standardized annual incidence risk of oral and pharyngeal cancers, classified by sex

Site	Sex	Crude Incidence	Standardized	
			Incidence	95% CI
Oral	Male	1.60	2.28	1.94-2.63
	Female	0.77	1.16	0.91-1.42
	Total	1.19	1.75	1.53-1.96
Pharyngeal	Male	0.36	0.49	0.34-0.65
	Female	0.30	0.40	0.26-0.54
	Total	0.33	0.45	0.34-0.55
All	Male	2.10	2.41	2.64-3.23
	Female	1.11	1.34	1.40-1.91
	Total	1.50	2.21	2.15-2.41

Direct method was used to standardize the incidence risks based on age and sex distribution of the standard world population

Table 2: The effects of sex and age on the risks of oropharyngeal cancer

Site		***Risk Ratio***	**95% CI**
Oral	Sex		
	Male	1	-
	Female	0.51	0.39-0.66
	Age		
	<40	1	-
	40-59	10.7	7.4-15.8
	>60	42.2	30.2-59.1
Pharyngeal	Male	1	-
	Female	0.85	0.53-1.35
	Age		
	<40	1	-
	40-59	6	3.5-10.3
	>60	9	5.1-16
All types	Male	1	-
	Female	0.57	0.46-0.72
	Age		
	<40	1	-
	40-59	8.9	6.5-12
	>60	29.3	2.3-38.7

Table 3: The mean age and the crude and standardized annual incidence risk of oral and pharyngeal cancers classified by location

	Site	**Crude incidence**	**standardized**		**Mean age (SD)**
			Incidence	**95% CI**	
Oral	Lip	0.5	0.8	0.6-0.9	62.6(14.94)
	Tongue	0.2	0.3	0.2-0.4	56.67(15.78)
	Gum	0.1	0.2	0.1-0.3	40.52(24.46)
	Floor of mouth	0.0	0.0	0.0-0.0	58(-)
	Other and unspecified parts of mouth	0.3	0.5	0.3-0.6	55.93(16.72)
	All Sites	1.19	1.75	1.53-1.96	57.3(17.9)
Pharyngeal	Oropharynx	0.1	0.1	0.0-0.2	39.62(23.38)
	Nasopharynx	0.2	0.3	0.2-0.4	43.63(19.51)
	Hypopharynx	0.0	0.0	0.0-0.0	45(13.83)
	Other and unspecified parts of mouth	0.1	0.1	0.0-0.2	56.33(16.49)
	All Sites	0.33	0.45	0.34-0.55	44.12(19.72)
Oropharyngeal		1.50	2.21	2.15-2.41	54.48(19.05)

Direct method was used to standardize the incidence risks based on age and sex distribution of the world population in 1995

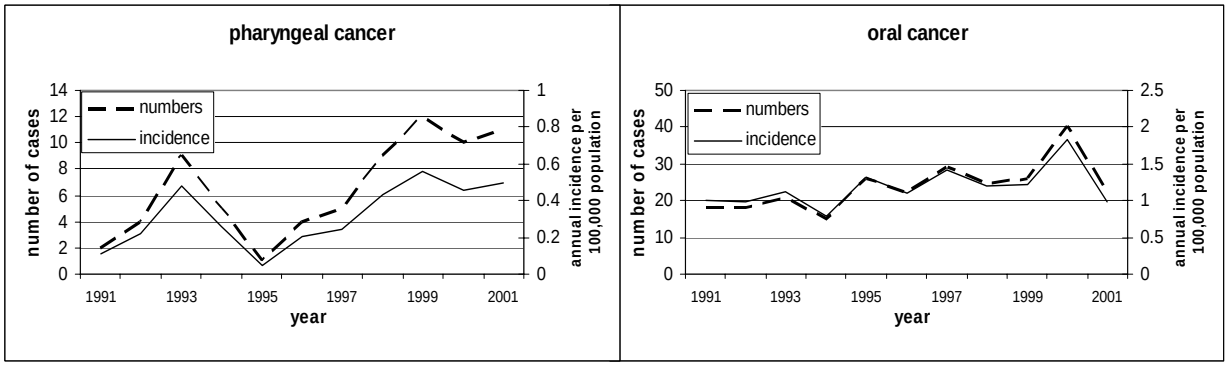

Fig. 1: The temporal variation of the annual incidence of pharyngeal and oral cancers.

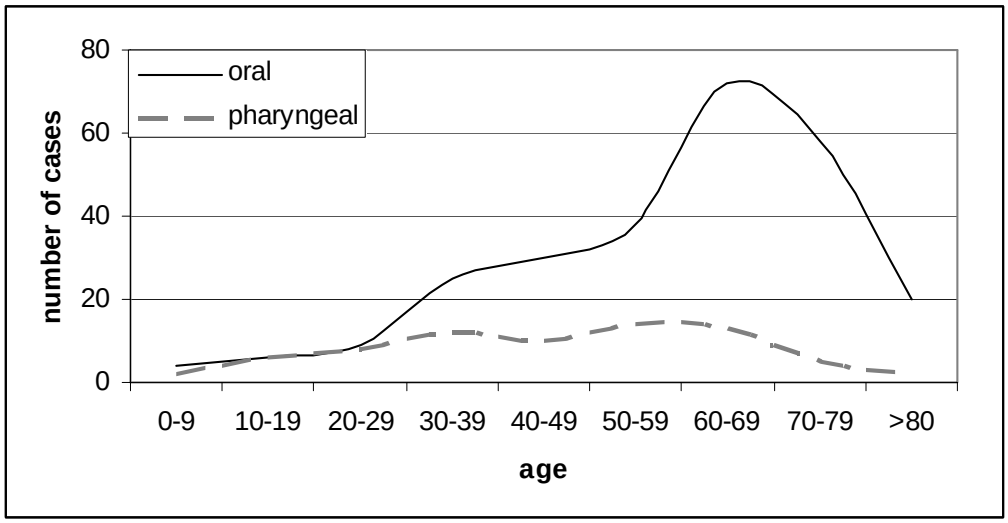

Fig. 2: Age distribution of oral and pharyngeal cancers

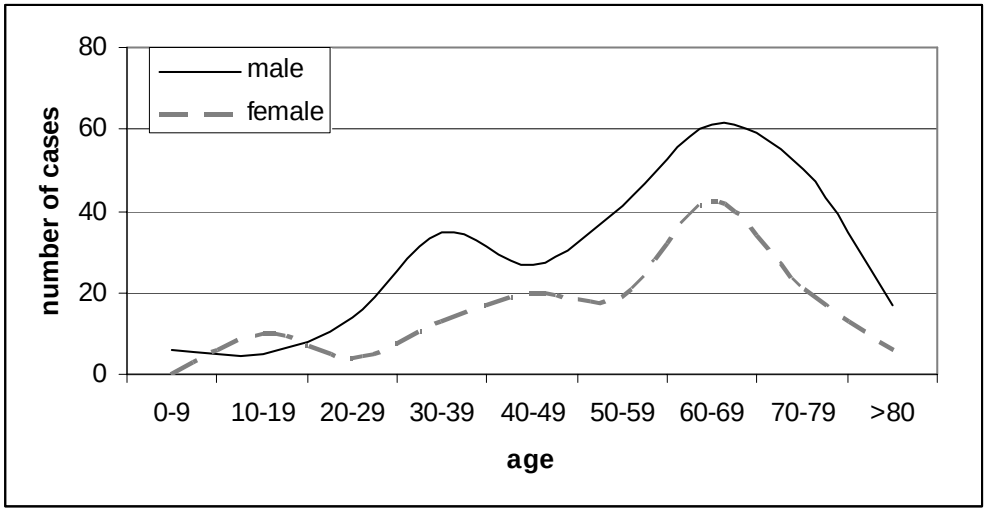

Fig. 3: Age distribution of oropharyngeal cancers, classified by sex.

Discussion

In this study the age adjusted annual incidence rate of oral cancers in Kerman was 1.75 per 100,000 population which was lower than the incidence rate in many parts of the world (8-10). In average, annual incidence of oral and pharyngeal cancers were increased 3 and 11 percent respectively between 1991 and 2001.The lip was the leading site of oral cancer. In addition, male to female ratio was around 2:1.

The incidence rate of oropharyngeal cancer in Iran is lower than the incidence rate in most parts of the world (9-11). The incidence of oral cancer in a neighboring province of Kerman (Fars Province) was 1.13 per 100,000 population, which is very close to the observed incidence rate in this study (12). The reported incidence in Bas Rhin, France (49.4/100,000 men), Slovakia (19.7/100,000 men) and Bombay, India (26.3/100,000 men) were much greater (10). The overall incidence of oral cavity and pharyngeal cancer in Kentucky, USA was 12.1/100,000 (13). Therefore, we may conclude that oropharyngeal cancer is less common in at least some parts of Iran.

We do not know why exactly the risk of oropharyngeal cancer is lower in our area; however, low alcohol consumption due to Islamic rules, and risky behaviors among people of this province such as chewing tobacco and eating spicy foods might explain some parts of this difference. In addition, since there is a synergic effect between alcohol consumption and smoking (6), low consumption of alcohol could lesson the impact of smoking as well. Moreover, tea is the most common hot drink in Iran which might protect people as well (14, 15). The relation of green tea consumption with oral carcinogenesis was examined in Japan and there was a tendency for a reduced risk of oral cancer in women (16).

We observed a slight increase in the incidence of oropharyngeal cancer between 1991 and 2001. It has been reported that increases in pharyngeal cancer in Japan and in most central, southern, and eastern European countries are likely to reflect increases in cigarette smoking, which have occurred since 1950 in men in such areas (17). Unfortunately, we did not have any accurate statistics about the prevalence of smoking in this period in Kerman Province. In addition, due to the time lag between exposure to smoking and cancer, we needed information about the history of smoking habits which was not available. Nevertheless, we should mention that improvement in cancer registry and recording might explain some part of this increase. It seems that more investigations are needed in this area regarding the suggestive role of oncogenic viruses such as the Epstein-Barr virus and human papillomavirus as risk factors for pharyngeal cancer (18-20).

In the present study, males were affected about two times as often as females. This ratio is similar to some other studies (21-24). In general, oral cancer occurs more frequently in males than females (22). Male predominance in some parts of the world, particularly in Taiwan can be as high as 15:1 (25). In the past two decades from 1982 to 2001, Taiwan had an alarming 5.3-fold increase in the incidence of male oral cancer (26). In certain high risk areas in South Asia and other south-east Asian countries like Singapore and Indonesia women seem to be at the same risk as men (27, 28). One explanation for this difference between sexes might be behavior exposure to some risk factors as tobacco and alcohol consumption and exposure to sunlight.

In the present study, the leading site of oral cancer was the lip. Lip cancer accounted for approximately half of the total oral malignancies, which was in accordance with a previously published report (22). The incidence of lip cancers shows large geographic variation with particularly high rates being reported in Australia, Canada and Eastern Europe. Lip malignancies have a very large reported incidence in Asian males, while in some areas (Singapore, Japan and China) lip cancer appears to be virtually unknown (29). Chronic exposure to solar radiation is commonly cited as the key etiologic agent in the development of lip cancer (30). The high frequency of lip

SCC in the present study especially in males might be attributed to ambient sun irradiation throughout the whole year at a generally high altitude and outdoor activities. It should be noted that 46% of our study population dweller in rural vicinities and many of them are farmers.

We collected the data of cases retrospectively; however since we could not collect data on potential risk factors, it was our main limitation. The coverage of our databank could be the other limitation in this study. Although, we searched all of the pathology centers in Kerman province to maximize the coverage and excluded repeated cases, we might have missed some unrecorded cases in this province. However, our findings are still valuable; since diagnostic facilities were well distributed around the whole province and due to a short waiting list people could receive affordable diagnostic and therapeutic care. We believe that most cases have some records in the histopathology centers that we covered even if the sough after treatment was in other cities such as Tehran. Nevertheless, such a potential selection bias may change the overall incidence rates, but their impacts on the RRs would be negligible.

The present study showed that the overall incidence rate of oral cavity and pharynx cancer in Kerman Province was lower than that in most parts of the world (annual incidence rate: 1.75 per 100,000 population) and this might be due to behavioral differences such as low consumption of alcohol, chewing tobacco, and spicy foods. The lip was the most common site of oral cancer which is mostly due to sunlight.

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The authors declare that there is no conflict of interests.

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