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Epidemiology of Head and Neck Cancers in Northern Iran: A 10-Year Trend Study From Golestan Province

Mohammad-Hossein Taziki, MD[1]; Abdolreza Fazel, MD[2*]; Fatemeh Salamat, MSc[1]; Seyed-Mehdi Sedaghat, MD[3]; Mohammad Ashaari, MD[4]; Hossein Poustchi, MD, PhD[5]; Ramin Shakeri, MD, PhD[5]; Reza Hoseinpoor, MSc[3]; Susan Hasanpour-Heidari, MSc[2]; Gholamreza Roshandel, MD, PhD[6]

[1]Cancer Research Center, Golestan University of Medical Sciences, Gorgan, Iran
[2]Golestan Research Center of Gastroenterology and Hepatology, Golestan University of Medical Sciences, Gorgan, Iran
[3]Deputy of Public Health, Golestan University of Medical Sciences, Gorgan, Iran
[4]Department of pathology, Golestan University of Medical Sciences, Gorgan, Iran
[5]Digestive Diseases Research Institute, Tehran University of Medical Sciences, Tehran, Iran
[6]Omid Cancer Research Center, Omid preventive medicine and health promotion center, Gorgan, Iran

Abstract

Background: Golestan province, in Northern Iran, is a high-risk area for esophageal squamous cell carcinoma (SCC). SCC is also the most common histological type of cancers of the head and neck region including cancers of oral cavity, oropharynx, hypopharynx and larynx. We aimed to present the incidence rate of head and neck SCC (HNSCC) in Golestan province during 2004 and 2013.

Methods: Data on HNSCC were obtained from Golestan population-based cancer registry (GPCR). Quality control and data analysis were performed using CanReg software. Age standardized incidence rates (ASRs) were calculated using the world standard population. The ASRs were presented per 100 000 person-years for different genders, residence places and years.

Results: During the 10-year period from 2004–2013, 434 cases of HNSCC were registered. 327 (75.3%) of these cases were male, 51.2% (222 cases) lived in urban areas and 351 (80.9%) of the total HNSCCs occurred in the larynx. Overall, the ASR of HNSCCs in Golestan province was 4.8. The ASR of HNSCCs was more than two-fold higher in male (6.6) than female (3.0). Our results showed an increasing trend in ASR of larynx cancer during the study period both in male and female.

Conclusion: We found relatively high rates of larynx cancer in Golestan province. Our results also showed higher rates of HNSCC in males and urban population. Considering common risk factors between HNSCCs and esophageal cancer, further studies are needed to clarify different aspects of HNSCCs (including epidemiology and risk factors) in this high-risk population.

Keywords: Golestan, Head and neck, Incidence rate, Iran, Neoplasms

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Introduction

Cancer is the third cause of death in Iran. Thus, it's one of the most important health problems in our country like other developed and developing countries. Recent studies have shown that 9007 new cases of cancer have been recorded according to the population-based cancer registry of northern Iran between 2004 and 2008. They have reported age-standardized rates of 175.30 and 141.10 per 100 000 person-years for females and males, respectively.[1]

Esophageal squamous cell carcinoma (SCC) as an upper gastrointestinal cancer is one of the most common cancers in northern Iran according to Golestan population-based cancer registry (GPCR) from 1970 to 2008.[1-3] Opium, tobacco and alcohol use, poor oral hygiene, obesity and drinking hot tea are the most important risk factors of this cancer.[4-6] The most common histological type of esophageal cancer especially in developing populations is SCC. Previous reports suggested that the histology of 90% of esophageal cancers in Golestan province were SCC.[4-6]

SCC is also the most common histological type of cancers of the head and neck region including cancers of oral cavity, oropharynx, hypopharynx and larynx. Therefore, malignant neoplasms of these organs may be categorized as head and neck SCC (HNSCC).

Different reports have suggested similar risk factors for esophageal cancers and the HNSCCs.[7–10] Therefore, epidemiological studies on HNSCC are important in areas with high incidence of esophageal cancer.[7-10]

Approximately 550 000 new cases of cancer occur each year in the world, and HNSCC is the sixth most common cancer. Incidence of HNSCC has a large variation all over the world, and it is mostly prevalent in Asia and

*Corresponding Author: Abdolreza Fazel, MD; Golestan Research Center of Gastroenterology and Hepatology, Golestan University of Medical Sciences, Gorgan, Iran. Address: Sayyad Shirazi Hospital, Sayyad Shirazi Bulevard, Gorgan, Iran. Tel. +98 1732251910 (Ext. 2637), Email: grcgh@goums.ac.ir.

northern Europe.[11]

HNSCC has a poor prognosis and has low 5-year survival rate over the past four decades, thus known as a major health problem.[7] In 2016, 61 760 new cases of HNSCC were diagnosed in the United States, and 13190 cases died.[10] HNSCC usually occurs in people over 60 years but, some reports suggested the occurrence of these cancers at earlier ages and young people in different parts of the world such as the United States, China, India and European countries.[12-16] Age of HNSCC occurrence in Iran is lower than other countries.[7] Poor prognosis and multiple risk factors in young adults show that there is a change in epidemiological features of disease, and physicians need to pay more attention to it.[17-21] The most common histologic type of HNSCC occurs in oral cavity, oropharynx, hypopharynx and larynx.[22] Tumor location in young adults is different from old patients. In young patients, tumors occur more in oropharynx and oral cavity than larynx.[7]

Given that incidence of esophageal cancer in northern Iran is high and most of its risk factors are similar to HNSCC, and up to now, no data have been reported on HNSCC in this region, we aimed to report 10-year incident rate of HNSCC in Golestan, Iran.

Materials and Methods

This cross-sectional study was conducted in Golestan province, in Northern Iran, during 2004–2013. All primary HNSCC recorded in GPCR were enrolled in this study. Tumor metastasis to other organs was not registered. International Association of Cancer Registries (IACR) standards were used to register malignant tumors. Cancers of organs related to HNSCC including oral cavity, oropharynx, hypopharynx and larynx were included in this analysis.

The detailed methodology of the GPCR was described elsewhere previously.[23] In brief, during 10 years (2004–2013), new cases of HNSCC collected by GPCR from all public and private diagnostic and health centers in Golestan including hospitals, pathology laboratories, diagnostic radiology clinics and some specialist physicians' offices enrolled in this study. We also collected information from medical centers and regional registries in neighboring provinces (Khorasan Razavi, Mazandaran and Tehran) to minimize the possibility of data loss.

Well trained staff working at the GPCR frequently visited these centers and collected the data of HNSCC cases. In some centers, data were collected previously. Information on cancer-related deaths was collected from death registry at the Health Department of Golestan University of Medical Sciences (GOUMS). Ten percent of questionnaires were rechecked with original documents to verify the accuracy of the information gathering process. Third edition of the International Classification of Diseases for Oncology (ICD-O) was used for coding anatomical site and histology of the tumor.[24] Duplicate reports were checked considering different variables (patient's full name, age, patient's father's name, topography of tumor, place of residence and year of disease diagnosis), and were removed before entering the database.

We entered the data in to the CanReg software and checked the data with IACR check program. We used the 18-groups world population (0–4, 5–9… >85) to calculate age standardized incidence rate (ASR) of HNSCC. ASR was reported per 100 000 person-years.

Data on Golestan population was achieved from statistics center in health department of GOUMS.

Results

During the 10-year period from 2004–2013, 434 (2.2%) of the total 19807 new cancer cases reported to the GPCR, were HNSCCs. Characteristics of patients including tumor location, diagnosis method, sex and residence area are displayed in Table 1. 327 (75.3%) cases were men and 107 (24.7%) were women. 351 (80.9%) cases of the total HNSCCs occurred in the larynx. 51.2% (222 cases) of HNSCC patients lived in urban areas and the remaining 212 patients were from rural areas. We found considerable increasing trend in the proportion of

Table 1. Characteristics of Patients With Head And Neck Squamous Cell Carcinomas According to Year of Diagnosis in Golestan, Iran, 2004–2013

Variable	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	Total
Organ, No. (%)											
Larynx	29 (85.3)	31 (91.2)	29 (70.7)	26 (83.9)	31 (79.5)	36 (72)	45 (78.9)	36 (81.8)	41 (80.4)	47 (88.7)	351 (80.9)
Oral cavity	4 (11.8)	1 (2.9)	8 (19.5)	2 (6.5)	6 (15.4)	10 (20)	9 (15.8)	4 (9.1)	5 (9.8)	2 (3.8)	51 (11.7)
Pharynx	1 (2.9)	2 (5.9)	4 (9.8)	3 (9.7)	2 (5.1)	4 (8)	3 (5.3)	4 (9.1)	5 (9.8)	4 (7.5)	32 (7.4)
Sex, No. (%)											
Male	26 (76.5)	26 (76.5)	27 (65.9)	21 (67.7)	30 (76.9)	39 (78)	44 (77.2)	36 (81.8)	38 (74.5)	40 (75.5)	327 (75.3)
Female	8 (23.5)	8 (23.5)	14 (34.1)	10 (32.3)	9 (23.1)	11 (22)	13 (22.8)	8 (18.2)	13 (25.5)	13 (24.5)	107 (24.7)
Residence area, No. (%)											
Urban	17 (50)	14 (41.2)	17 (41.5)	19 (61.3)	13 (33.3)	18 (36)	27 (47.4)	23 (52.3)	31 (60.8)	33 (62.3)	222 (51.2)
Rural	17 (50)	20 (58.8)	24 (58.5)	12 (38.7)	26 (66.7)	32 (64)	30 (52.6)	21 (47.7)	20 (39.2)	20 (37.7)	212 (48.8)

patients from urban area as well as a decreasing trend in the proportion of patients from rural area.

In majority of HNSCC cases (70.0%), the diagnosis of cancer was confirmed by pathological methods. The diagnosis in 50 (11.5%) patients was made by death certificate only (DCO) method. The methods of diagnosis in different subtypes of the HNSCCs are presented in Table 2.

Overall, the ASR of HNSCCs in Golestan province was 4.8 per 100 000 person-year. The ASR of HNSCCs was more than two-fold higher in males (6.6 per 100 000 person-year) than females (3.0 per 100 000 person-year) (Table 3). The difference in incidence rate between males and females was significant only for the larynx cancer (P = 0.03). But, there was no significant difference in the incidence of cancers of the oral cavity and pharynx between two genders (Table 3).

Table 4 shows the temporal trends in ASR of subtypes of HNSCCs in males and females during 2004 and 2013. The results suggest increasing trends in ASR of larynx cancer during the study period both in males and females.

The ASRs and age specific incidence rates (per 100 000 person-year) of HNSCCs in males and females during the 10-year period are shown in Figures 1 and 2, respectively. Overall, there was no significant trend in ASR of the HNSCCs during the study period.

Table 2. Distribution of Head and Neck Squamous Cell Carcinomas (HNSCC) According to Diagnosis Methods in Golestan, Iran, 2004–2013

Organ	Diagnostic Methods	No.	%
Larynx	Death certificate only	48	13.7
	Clinical/paraclinical	70	19.9
	Pathology	233	66.4
Oral cavity	Death certificate only	0	0
	Clinical/paraclinical	10	19.6
	Pathology	41	80.4
Pharynx	Death certificate only	2	6.2
	Clinical/paraclinical	0	0
	Pathology	30	93.8
All HNSCCs	Death certificate only	50	11.5
	Clinical/paraclinical	80	18.4
	Pathology	304	70.1

Discussion

The results of this study showed that 434 (2.2%) of 19807 new cases of cancer registered in GPCR during 2004-2013 were HNSCCs. Our findings suggested an overall ASR of HNSCCs as 4.8 per 100 000 person-year. The ASRs of HNSCCs were 6.6 and 3 per 100 000 person-year in males and females, respectively. Our results suggested that the incidence rates of cancers of the oral cavity, pharynx and larynx in males were 1.5, 0.2 and 4.9, and in females were 1.5, 0.4 and 1.1 per 100 000 person-year, respectively.

Generally, in global cancer statistics, the highest oral cavity cancer rates are found in Melanesia, South-Central Asia, and Central and Eastern Europe, and the lowest are found in Africa, Central America, and Eastern Asia for both males and females.[11,25] Smoking, alcohol use, using smokeless tobacco products, and HPV infections are the major risk factors for oral cavity cancer, with smoking and alcohol having synergistic effects.[26,27] The contribution of each of these risk factors varies across regions because of differences in lifestyles.[26,28]

According to the report of the Globocan-2012 project, in 2012, 529 500 patients were newly diagnosed with HNSCC globally, of whom 375 000 (70.8%) were

Table 3. Age Standardized Incidence Rates (ASR) (Per 100 000 Persons-Year) of Head and Neck Squamous Cell Carcinomas in Urban and Rural Areas of Golestan Province in Iran During 2004–2013

Organ	Male		Female		Total	
	Number of Cases	ASR	Number of Cases	ASR	Number of Cases	ASR
Oral cavity						
Urban	13	1.4	12	1.7	25	1.55
Rural	15	1.6	11	1.5	26	1.55
Total	28	1.5	23	1.5	51	1.5
Pharynx						
Urban	3	0.1	9	0.3	12	0.2
Rural	13	0.4	7	0.3	20	0.35
Total	16	0.2	16	0.4	32	0.3
Larynx						
Urban	142	4.8	33	1.1	175	2.95
Rural	141	5	35	1.2	176	3.1
Total	283	4.9	68	1.1	351	3
Total						
Urban	158	6.3	54	3.1	212	4.7
Rural	169	7	53	3	222	5
Total	327	6.6	107	3	234	4.8

Table 4. Age Standardized Incidence Rates (ASR) (Per 100000 Persons-Year) of Head and Neck Squamous Cell Carcinomas According to Year of Diagnosis in Golestan Province in Iran During 2004–2013

	2004		2005		2006		2007		2008		2009		2010		2011		2012		2013	
	No. of Cases	ASR	No. of Cases	ASR	No. of Cases	ASR	No. of Cases	ASR	No. of Cases	ASR	No. of Cases	ASR	No. of Cases	ASR	No. of Cases	ASR	No. of Cases	ASR	No. of Cases	ASR
Male																				
Oral Cavity	1	1.8	1	2.2	4	1.7	0	1.4	5	1.7	6	1.9	5	1.3	3	1.2	2	1.2	1	1.4
Pharynx	1	0.2	1	0.1	3	0.6	1	0.2	1	0.1	1	0.1	2	0.1	3	0.3	2	0.3	1	0.1
Larynx	24	4.4	24	4.8	20	3.9	20	3.8	24	4.3	32	5.9	37	6	30	5.1	34	5.1	38	5.2
Female																				
Oral Cavity	3	2.3	3	0.2	4	1.7	2	2	1	1.5	4	2.2	4	2.1	1	0.7	3	1.6	1	0.8
Pharynx	0	0	0	0.2	1	0.4	2	0.2	1	0.1	3	0.7	1	0.4	1	0.1	3	0.5	3	0.3
Larynx	5	0.8	5	1.4	9	1.9	6	1	7	1.2	4	0.6	8	1.4	6	1	7	1.1	9	1.2

men and 154400 (29.2%) were women.[29] The global incidence of cancers of oral cavity, pharynx and larynx in the world's male population was 5.5, 4.9 and 3.9 and in the world's female population was 2.5, 1.4 and 0.5 per 100000 person-year, respectively.[25] In the United States, in 2014, 54000 new cases of HNSCC occurred, and annual incidence was 15 per 100000. In Europe, HNSCC incidence rate was higher, with 140000 new cases diagnosed in 2014, and annual incidence of 43 per 100000.[30] India has the world's highest incidence rates of the lower pharynx cancer (11.5 per 100000) and tongue cancer (7.6 per 100000), and also the highest incidence rate of mouth cancer among males (8.9 per 100000).[31] Therefore, the incidence of cancers of the oral cavity and pharynx were considerably lower in our population compared to the world's population. On the other hand, we found a higher rate of larynx cancer compared to the world's population. Regarding the high incidence of esophageal cancer in Golestan province, the high rate of larynx cancer in this region may partly be explained by higher prevalence of common risk factors of the esophageal and larynx cancers in this population including opium, tobacco and alcohol use, poor oral

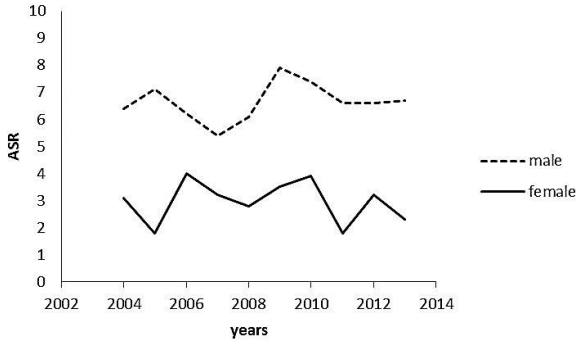

Figure 1. Age Standardized Incidence Rates (ASR) (Per 100000 Persons-Year) of Head and Neck Squamous Cell Carcinomas (HNSCC) in Males and Females in Golestan Province in Iran During 2004–2013.

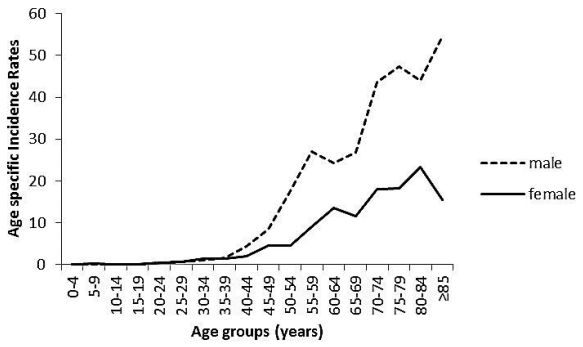

Figure 2. Age Specific Incidence Rates (Per 100000 Persons-Year) of Head and Neck Squamous Cell Carcinomas (HNSCC) in Males and Females in Golestan Province in Iran During 2004–2013.

hygiene, obesity, and drinking hot tea.[4-6] Further studies are needed to clarify this important point in this high-risk population.

According to the results of this study, most of the cases were occurred in men (327 (75.3%)). The ASRs of HNSCCs were 6.6 and 3.0 per 100 000 person-year in male and female, respectively. The difference in incidence rates between males and females was significant only for the larynx cancer. But, there was no significant difference in incidence of cancers of the oral cavity and pharynx between two genders. Results of a study in Shiraz, Iran showed that 145 out of 3708 new cases (3.97 percent) were HNSCCs during 2002–2003. In this study, the incidence of HNSCC in men was also higher than in women.[32] Another study in Tehran, Iran reported 262 new cases of HNSCCs within 1992–2007, suggesting the highest incidence of larynx cancer (74.04%) in men.[33] Approximately 90% of patients with HNSCCs have a history of tobacco use. Patterns of tobacco use have influenced on incidence of HNSCCs. In developed countries, approximately 75% of HNSCCs is attributed to tobacco smoking and alcohol consumption. High tobacco consumption rate In Eastern Europe and China causes a rise in HNSCC. Also, alcohol use increases the risk of HNSCCs; it specifically increases the risk of hypopharyngeal cancer. In developing countries, risk factors for lip, oral cavity, oropharyngeal and pharyngeal cancers also include betel quid chewing with or without tobacco and the use of pipes. Men have a 2- to 5-fold greater risk of HNSCC than women. Higher risk of HNSCCs in men compared with women is likely due to more exposure to these risk factors in men.[22,30,34]

According to the results of our population-based study, there were considerable temporal changes in the proportions of HNSCCs in urban and rural areas. During the earlier years of the study, the proportions of the cases in urban and rural areas were almost the same. But, we found increasing trends in the proportions of HNSCCs in urban population in the latter years. These temporal trends may partly be explained by changes in lifestyle and migration to urban areas and exposure to new city's risk factors. Results of some epidemiological studies have shown that some important risk factors for HNSCCs including smoking, alcohol use, use of preserved food, lack of physical activities, overweight, low intake of fruit and vegetables and exposure to industrial and environmental carcinogens may be associated with urbanization.[34] Therefore, increasing trend of HNSCC in urban population should be considered in planning cancer control programs, especially in developing countries.

In conclusion, our findings suggested relatively high rates of larynx cancer in Golestan province. We also found higher rates of HNSCC in males and urban population. Regarding high incidence rate of esophageal cancer in Golestan province in Iran, and considering common risk factors between HNSCCs and esophageal cancer, further studies are needed to clarify different aspects of HNSCCs (including epidemiology and risk factors) in this high-risk population.

Authors' Contribution

MT and AF: conceptualized and designed the study; critically reviewed manuscript; FS and SH: wrote the first draft of manuscript; SS, MA and RH: collaborated in collection of data and data processing; HP and RS: interpreted data; Edited and critically reviewed manuscript; GR: performed statistical analysis; interpreted results; All authors read and approved the final manuscript.

Conflict of Interest Disclosures

The authors have no conflicts of interest.

Ethical Statement

The study protocol was approved by the ethics committee of Golestan University of Medical Sciences.

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