



Incidence of Esophageal Cancer in Iran, a Population-Based Study: 2001–2015

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Abstract

Purpose Even though Kurdistan, the western province of Iran, has a cancer surveillance system, a detailed analysis of incidence rate has not been yet performed. We describe Age Standardized Incidence Rates (ASRs) for esophageal cancer (EC) in Kurdistan Province of Iran in 2001–2015.

Methods Incidence cases of EC were obtained from a population-based cancer registry. We obtained ASRs and 95% confidence intervals (CI) per 100,000 populations for each calendar year group.

Results Between 2001 and 2015, 1362 incidence cases with EC were reported to the cancer registry. Annual ASRs in 2006–2010 were more than the other years in both men and women, respectively. Most ASRs were reported among women in Divandarreh (18.95, 95% CI 14.76, 23.92), Saqez (12.75, 95% CI 10.73, 15.01), Sanandaj (8.84, 95% CI 7.64, 10.17), and Qorveh (8.19, 95% CI 6.54, 10.12), and among men in Divandarreh (19.38, 95% CI 15.38, 24.06), Saqez (13.64, 95% CI 11.49, 16.05), Sanandaj (8.70, 95% CI 7.56, 9.96), and Marivan (7.93, 95% CI 6.26, 9.88).

Conclusions It was concluded that EC in Divandarreh, Saqez, and Sanandaj has the highest ASRs, and these areas are considered as high-risk areas for this disease in the Iranian province of Kurdistan. Therefore, to understand the reasons of these problems, a considerable work is needed.

Keywords Esophageal · Cancer · Iran · Kurdistan · Incidence

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Introduction

Esophageal cancer (EC) is considered as the ninth common cause of cancer-related death worldwide [1]. In 2015, there were 17.5 million cases of cancer worldwide; and Age Standardized Incidence Rate (ASR) for EC was 11.6 (95% confidence interval (CI) 10.3–13.7) [2]. The overall survival ranges for EC were from 15 to 25% at 5 years [3]. EC survival decreased to 7% per year after 5 years [4]. Incidence of EC varies by region; Asian belt including Iran has a very high incidence rate of EC [3]. In Iran, the peak of ASR was 5.62 per 100,000 populations in 2001–2010 [5]. There is an obvious geographic difference in the incidence of EC in different parts of Iran [6]. Golestan Province located in northeastern Iran is considered as a high incidence area for EC [7]. Moreover, ASR of EC in Kerman province in south of Iran, as a low incidence area, was 1.9 per 100,000 populations [8]. This evidence may indicate that risk factors for EC are different in different regions of Iran [6]. Tobacco, alcohol consumption, symptomatic gastro-esophageal reflux disease, low socioeconomic status, poor oral health, obesity, and nutritional

deficiencies are the most important risk factors for EC [3, 7, 9].

Considerable variations in incidence rates in Iranian provinces may provide more opportunity for generating hypotheses to determine the factors affecting provincial differences. In addition, although the province of Kurdistan in western Iran has a cancer registry surveillance system, so far, there has not been any detailed research on ASR. Therefore, in this research, ASR for EC is described in Kurdistan province in 2001–2015 in general and for urban populations based on age, sex, and calendar year.

Methods

Data Source

Kurdistan province is one of 31 provinces of Iran. It is located in the west of the country with an area of 28,817 km². Most residents of this province speak Kurdish. The capital of Kurdistan province is Sanandaj, and other major cities of the province include Baneh, Bijar, Divandarreh, Kamyaran, Marivan, Qorveh, and Saqez (Fig. 1).

EC incidence cases of Kurdistan Province, by major cities of Sanandaj, Baneh, Bijar, Divandarreh, kamyaran, Marivan, Qorveh, and Saqez, were obtained from a population-based cancer registry. The dataset comprised of 1362 reported cases with the date of diagnosis between March 21, 2001, and March 20, 2015. The data were classified according to the age group of ten and sex. But this grouping is different for people under the age of 30 and above 85. As few EC cases have been reported for several years, the incidence rate has been reported in 5-year periods of 2001–2005, 2006–2010, and 4-year period of 2011–2015. In the Iranian surveillance system, cases of cancer are reported to the Vice-Chancellery for Health in the provincial capital, by provincial pathology labs and health organizations outside the province.

Age at diagnosis, sex, and International Classification of Disease (ICD-10) code C15 were extracted from cancer registry center. For confidentiality, we analyzed the extracted data to remove duplicate records. Duplicate records were excluded from the analysis.

Population Data

We calculated mid-year population estimates for the province of Kurdistan from the Iranian website of Statistics Center [10]. In this center, the population and housing statistics in 1996, 2006, 2011, and 2016 is presented on the basis of age and gender. We obtained mid-year population estimates based on census data of (1996, 2006), (2006, 2011), and (2011, 2016) for the denominators of incidence rates between 2001 and 2005, 2006 and 2010, and 2011 and 2015, respectively.

Statistical Analysis

Age Standardization

Incidence case and population data were arranged based on age groups of ten and sex. We obtained Age Standardized Incidence Rate (ASR) and 95% confidence intervals (CI) per 100,000 for each calendar year group using the direct method provided by the world standard population by Segi and Doll [11–13] and calendar year group specific crude rates. The STATA 14.0 software was used to obtain ASR [14] at the urban level for Kurdistan province. Annual incidence rates per 100,000 during the period 2001–2015 have been calculated based on the number of cases and corresponding mid-year population estimates produced by the Population and Housing Census. The map of the cities of Kurdistan was drawn by ArcMap 10.0 software.

Ethical Considerations

This study was conducted in compliance with the provisions of the Helsinki Declaration. The protocol was approved by the Ethics committee of Arak University of Medical Sciences, Arak, Iran, with the ethical code IR.ARAKMU.REC.1394.384.

Results

Between 2001 and 2015, 1362 incidence cases with EC were reported to the Kurdistan province cancer registry. Median ages at diagnosis were 65 and 69 years in women and men. Moreover, EC was reported in 47% ($N = 645$) and 53% ($N = 717$) of women and men, respectively. The ratio of men to women was 1.1:1.

In Kurdistan province, in 2001 to 2015, the annual ASRs was 8.87 (95% CI 8.23, 9.56) and 8.57 (95% CI 7.91, 9.26) per 100,000 person-years in males and females, respectively (Table 1). In 2006–2010, annual ASRs were more than other year-groups in both men and women (9.98, 95% CI 8.82, 11.24 and 9.42, 95% CI 8.28, 10.64, respectively).

Table 2 shows incidence cases, number of population, and ASRs by urban and year groupings. According to Table 2, between 2006 and 2010, ASR among women in Baneh, Kamiaran, Qorveh, Sanandaj, and Saqez, and among men in Baneh, Kamiaran, Marivan, and Qorveh, was higher than the other years.

In 2001–2005, the most ASRs were reported in women in Divandarreh (17.1, 95% CI 10.40, 26.34), Saqez (14.92, 95% CI 10.98, 19.76), and Sanandaj (9.10, 95% CI 6.78, 11.92) and in men in Divandarreh (19.92, 95% CI 13.08, 28.92), Saqez (17.18, 95% CI 12.76, 22.52), and Marivan (7.88, 95% CI 5.12, 11.58), respectively.

Fig. 1 Map of the cities of Kurdistan, Iran



In 2006–2010, the highest ASRs for EC were occurred in Divandarreh (17.70, 95% CI 11.50, 25.92), Saqez (13.58, 95% CI 10.20, 17.66), and Qorveh (11.60, 95% CI 8.46, 15.46) for women and in Divandarreh (17.72, 95% CI 11.52, 25.90), Saqez (13.74, 95% CI 10.14, 18.10), and Baneh (10.70, 95% CI 5.94, 17.40) for men.

In 2011–2015, the most ASRs were raised among women in Divandarreh (18.18, 95% CI 11.63, 27.00), Saqez (10.20, 95% CI 7.20, 13.95), and Marivan (7.08, 95% CI 4.55, 10.45) and among men in Divandarreh (19.00, 95% CI 12.28, 27.95), Saqez (11.80, 95% CI 8.55, 15.88), and Sanandaj (10.30, 95% CI 8.23, 12.73).

In all years of study, between 2001 and 2015, most ASRs were reported among women in Divandarreh (18.95, 95% CI 14.76, 23.92), Saqez (12.75, 95% CI 10.73, 15.01), Sanandaj

(8.84, 95% CI 7.64, 10.17), and Qorveh (8.19, 95% CI 6.54, 10.12) and among men in Divandarreh (19.38, 95% CI 15.38, 24.06), Saqez (13.64, 95% CI 11.49, 16.05), Sanandaj (8.70, 95% CI 7.56, 9.96), and Marivan (7.93, 95% CI 6.26, 9.88).

Finally, it may be said that EC in Divandarreh, Saqez, and Sanandaj has the highest ASRs and they are considered as high-risk areas of this disease in the province of Kurdistan.

Discussion

In both sexes, we found that ASRs of EC were substantially more common in Divandarreh, Saqez, and Sanandaj. The ASRs of EC were lower in Baneh, Kamiaran, and Bijar. Their reasons are not clear but probably reflect a variety in

Table 1 Age Standardized Annual Incidence Rates of esophagus cancer in the Kurdistan Province, Iran in 2001–2015

Year	Female					Male				
	Incid. ^a	N ^b	Crude ^c	ASIR ^d	95% CI ^e	Incid. ^a	N ^b	Crude ^c	ASIR ^d	95% CI ^e
2001–2005	192	685,827	5.60	9.20	7.92, 10.6	217	707,433	6.14	9.02	39.2, 10.34
2006–2010	278	726,439	7.66	9.98	8.82, 11.24	272	740,367	7.34	9.42	41.4, 10.64
2011–2015	175	764,697	5.73	6.43	5.48, 7.45	228	780,220	7.30	8.30	28.9, 9.50
Total	645	724,086	6.36	8.57	7.91, 9.26	717	747,285	6.85	8.87	115.2, 9.56

^a Incidence number

^b Total number of population

^c Crude incidence rate

^d Age Standardized Annual Incidence Rate

^e Confidence interval

Table 2 Age Standardized Annual Incidence Rates of esophagus cancer in the cities of Kurdistan Province, Iran, in 2001–2015

City	Year	Female					Male				
		Incid. ^a	N ^b	Crude ^c	ASIR ^d	95% CI ^e	Incid. ^a	N ^b	Crude ^c	ASIR ^d	95% CI ^e
Baneh	2001–2005	6	54,503	2.20	3.28	1.08, 7.36	9	57,633	3.12	6.24	2.52, 12.32
	2006–2010	16	61,598	5.20	8.40	4.72, 13.60	20	64,010	6.24	10.70	5.94, 17.40
	2011–2015	5	71,742	1.75	2.20	.63, 5.30	5	73,878	1.70	2.55	0.75, 6.00
	Total	27	64,647	2.99	4.44	2.88, 6.49	34	67,501	3.60	5.58	3.69, 8.01
Bijar	2001–2005	15	53,609	5.60	7.28	4.06, 11.98	14	52,466	5.34	6.58	3.56, 11.04
	2006–2010	15	48,349	6.20	6.10	3.38, 10.10	14	47,464	5.90	5.54	2.96, 9.44
	2011–2015	5	45,716	2.73	2.20	.70, 5.23	7	45,722	3.83	3.80	1.53, 7.75
	Total	35	50,976	4.91	5.40	3.75, 7.51	35	50,723	4.93	5.17	3.59, 7.21
Divandarreh	2001–2005	20	41,951	9.54	17.10	10.40, 26.34	27	42,910	12.58	19.92	13.08, 28.92
	2006–2010	26	41,231	12.62	17.70	11.50, 25.92	28	41,897	13.36	17.72	11.52, 25.90
	2011–2015	24	38,406	15.63	18.18	11.63, 27.00	27	39,249	17.20	19.00	12.28, 27.95
	Total	70	39,126	12.78	18.95	14.76, 23.92	82	40,262	14.55	19.38	15.38, 24.06
Kambaran	2001–2005	4	50,767	1.58	3.08	.84, 7.58	8	52,800	3.04	4.24	1.78, 8.44
	2006–2010	9	52,122	3.46	4.84	2.18, 9.12	13	53,819	4.84	5.10	2.64, 8.90
	2011–2015	6	51,125	2.93	3.45	1.25, 7.45	8	53,296	3.75	3.70	1.53, 7.50
	Total	19	49,770	2.73	4.01	2.41, 6.22	29	52,277	3.96	5.12	3.41, 7.34
Marivan	2001–2005	22	95,967	4.58	8.74	5.46, 13.18	26	100,642	5.16	7.88	5.12, 11.58
	2006–2010	18	104,756	3.44	4.92	2.86, 7.80	33	108,596	6.08	9.26	6.30, 13.06
	2011–2015	25	112,788	5.55	7.08	4.55, 10.45	20	116,613	4.30	5.93	3.60, 9.13
	Total	65	104,000	4.46	7.00	5.38, 8.92	79	108,659	5.19	7.93	6.26, 9.88
Qorveh	2001–2005	23	100,491	4.58	7.56	4.78, 11.34	27	99,237	5.44	7.70	5.04, 11.24
	2006–2010	47	100,757	9.32	11.60	8.46, 15.46	36	98,955	7.28	8.32	5.76, 11.62
	2011–2015	16	100,526	3.98	4.58	2.60, 7.40	23	101,479	5.68	6.65	4.18, 9.98
	Total	86	100,260	6.13	8.19	6.54, 10.12	86	101,760	6.04	7.88	6.30, 9.72
Sanandaj	2001–2005	52	188,610	5.52	9.10	6.78, 11.92	47	199,966	4.70	6.76	4.94, 9.02
	2006–2010	90	213,248	8.44	11.24	9.00, 13.82	74	220,387	6.72	8.54	6.64, 10.78
	2011–2015	54	235,378	5.73	6.28	4.68, 8.20	89	240,370	9.25	10.30	8.23, 12.73
	Total	196	210,740	6.64	8.84	7.64, 10.17	210	219,949	6.82	8.70	7.56, 9.96
Saqez	2001–2005	50	99,932	10.00	14.92	10.98, 19.76	59	101,780	11.60	17.18	12.76, 22.52
	2006–2010	57	104,380	10.92	13.58	10.20, 17.66	54	105,240	10.26	13.74	10.14, 18.10
	2011–2015	40	109,018	9.18	10.20	7.20, 13.95	49	109,615	11.18	11.80	8.55, 15.88
	Total	147	104,570	10.04	12.75	10.73, 15.01	162	106,155	10.90	13.64	11.49, 16.05

^a Incidence number^b Total number of population^c Crude incidence rate^d Age Standardized Annual Incidence Rate^e Confidence interval

prevalence of risk factors. In Taiwan [15], ASR (at standard world population) was 8.04 in 1999 to 2003 that was considerably less than the high-risk area in this study. On the worldwide available information [16], ASRs per 100,000 for EC for both sexes from 1990 to 2013 were 9 and 4, respectively, for developing and developed countries, whereas the ASRs for EC in Divandarreh and Saqez is generally greater than developing countries. Among the countries of Western Asia, Iran is the most common country for EC; ASR in men and women

was 9 and 8, respectively [17]. In Tehran, Iran, during 1998–2001, ASRs in males and females were 6.8 and 5.3, respectively [18], while ASRs are relatively higher in Kurdistan province. In another study [19], between 1998 and 2002 in Fars, a southern province of Iran, calculated ASRs in women and men were 1.4 (95% CI 1.0, 1.7) and 2.0 (95% CI 1.6, 2.3) per 100,000 person-years referred to world standard population, respectively, whereas the ASRs are clearly higher in Kurdistan province. The difference in ASRs between

provinces may be due to differences in the prevalence of environmental factors such as dietary habits, smoking, and other risk factors.

Infection with helicobacter pylori, smoking, obesity, and gastro-esophageal reflux disease are possible risk factors for EC [7]. Despite these correlations between EC and the risk factors mentioned in many studies [20–22], no information is available on the prevalence of environmental risk factors in these high-risk areas. However, a number of studies have been conducted in Iran, and in them, the relationship between EC and opium use [6, 23, 24], smoking [6], family history of cancer [25], drinking hot tea [22], socioeconomic status [26], consumption of red meat [27], drinking un-piped water [27], and obesity [7] has been reported. A study conducted in a high risk area for EC in Iran, Golestan province, showed that the opium use and smoking are associated with EC [23]. In another province of Iran, Kerman, the incidence of EC is also relatively high and its prevalence is similar to opium use. On the other hand, it has been reported that opium use among rural men in the southern area of Iran was 17.3% [24]. A cross-sectional study in India showed a positive association between family history of cancer and EC [25]. In a high-risk area of Iran, it was found that red meat consumption above the third quartile (odds ratio (OR) 2.58, 95% CI 1.21, 6.57) and drinking un-piped water (OR 4.25, 95% CI 2.33, 8.11) increased odds of EC. Also, in this case-control study, fish intake has decreased EC. These risk factors may due to the possible nitrate combination of soil and water, be of interest for future studies [27]. In a case-control study conducted in Golestan province, an area with high incidence of EC, drinking hot or very hot tea was associated with EC [22].

Another important risk factor for EC is the socioeconomic status of subjects. Islami et al. [26] obtained strong inverse associations between education, wealth, marital status, and the incidence rate of EC. Obesity is one the most important risk factors for EC [7]. According to Emamian et al. [28], the prevalence of obesity in cities is higher than in rural areas; moreover, the majority of the Kurdistan population live in rural areas, so further studies in these areas may provide more clear evidence of an association between obesity and EC.

The first limitation of this study was the relatively poor quality of medical records in private pathology centers, hospitals, and other centers that may be due to the over or under-reported ASRs. Due to these reasons, to remove duplicates from this dataset, we order name and surname variables alphabetically to find similar names, even with this action, the names, or surnames of some cases may be mistakenly recorded and we could not do anything to find them, so these events may cause misclassification bias in the estimated incidence rates [29]. The second limitation was related to insufficient coverage of all occurred cases of EC in Kurdistan province by cancer registry because some patients seek the medical cares out of the Kurdistan province or in the other major cities;

like Tehran, the capital of Iran, as long as the patients' address in the clinic or pathological centers of the referred cities recorded incorrectly, an under-reported estimation in incidence cases may be occurred. Such issues may have occurred with the residents of Qorveh, Kamiaran, and Bijar because they are commonly pursuing their medical services respectively in the provinces of Hamedan, Kermanshah, and Zanjan. Despite these limitations, at least, we are sure that the estimated ASRs in these studies are minimum ASRs of EC in the cities of Kurdistan provinces.

For future research, it is recommended to focus on the cause of more incidence of EC in the population of Divandarreh and Saqez. Also, according to the results of this research, it is recommended for health policies to modify the potentially lifestyle related to risk factors identified in other studies worldwide, including high consumption of fatty and salty foods, high nitrate in soil and water of areas, opium use, smoking, obesity, and low consumption of fruits and vegetables.

It may be concluded that EC in Divandareh, Saqez, and Sanandaj has the highest ASRs and are considered high-risk areas in Kurdistan province. Therefore, a significant work is needed to understand the causes of these issues.

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Compliance with Ethical Standards

This study was conducted in compliance with the provisions of the Helsinki Declaration. The protocol was approved by the Ethics committee of Arak University of Medical Sciences, Arak, Iran, with the ethical code IR.ARAKMU.REC.1394.384.

Conflict of Interest The authors declare that they have no conflict of interest.

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