



Burden of esophageal cancer in Iran during 1995-2015: Review of findings from the Global Burden of Disease studies

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Abstract

Background: Iran is located in Asian esophageal cancer belt, with age-standardized incidence rate (ASR) of approximately 7 per 100,000 for both men and women. To provide potential solution recommendations for achieving accurate estimations regarding the burden of the disease in Iran, we designed a study to assess the burden of esophageal cancer in Iran during 1995-2015 by collecting data from the Global Burden of Disease studies.

Methods: Data were extracted from the Global Burden of Disease (GBD) during 1995-2015, which were published by the Institute for Health Metrics and Evaluation. For this purpose, disability adjusted life years (DALYs), incidence, and prevalence rate were applied to report burden of esophageal cancer based on gender and age group in Iran during 1995-2015. The Cochran-Armitage and t test were used to assess statistical significance. Stata Version 13 and Excel 2016 were used for data analysis.

Results: During 1995-2015, in total, 304 102 DALYs (179 562 for males vs. 124 540 for females) were attributed to esophageal cancer in Iran. In both genders and all ages, the number of DALYs increased significantly from 45 018 in 1995 to 74 399 in 2015.

Conclusion: Esophageal cancer is still a public health issue in Iran. Most of DALYs were due to years of life lost (YLL), suggesting the need for prevention, early detection, and screening programs. P-value was statistically significant just between male and female groups ($p < 0.05$).

Keywords: Esophageal cancer, Disability adjusted life years, Iran, Global burden of disease

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Introduction

Esophageal cancer is considered as a fatal disease in developed and developing countries. This health problem is the sixth most common cause of mortality due to cancer worldwide, with estimated 439 025 deaths in 2015 (1-3). Based on GLOBOCAN 2012 data, the estimated mortality rate of esophageal cancer is 14.1 per 100 000 in Eastern Asia, 12.8 in males in Southern Africa, 7.3 in Eastern Africa, and 6.2 in females in Southern Africa (1).

Iran is a country located in Asian esophageal cancer belt, with age-standardized incidence rates (ASR) of ap-

proximately 7 per 100 000 for males and females, which even exceeds 100 in its high-risk area (4-6). For instance, in Golestan province, in the eastern part of the Caspian littoral of Iran, the age-adjusted incidence rate has been reported to be 100 per 100 000 (World Standard Population) in the 1960s and 1970s for both genders. Other studies also showed age-standardized incidence rates of 43.4 and 36.3 for males and females, respectively during 1996-2000 (7, 8). Esophageal cancer is responsible for almost 5800 of 35 000 annual cancer deaths in Iran (9). Although

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↑What is "already known" in this topic:

In the last decade, the burden of esophageal cancer has increased in Iran, especially in males, and this cancer was the sixth most common cause of mortality due to cancer worldwide.

→What this article adds:

Esophageal cancer is common in Iran, and the majority of DALY due to esophageal cancer is related to 50-69 age group. The burden of esophageal cancer is significantly higher in males.

survival rate for cancers has been improving in recent years, esophageal cancer remains one of the most fatal malignancies. This cancer is diagnosed at a late stage, with 5-year survival rate of 10% and 14% for males and females, respectively, in Iran and 12% in Europe (10-12).

According to the literature relevant to esophageal cancer in Iran, studies that calculated the burden of esophageal cancer are divided into 2 groups. The first group, which is also the main group, includes studies using the number of deaths, prevalence, incidence rate, and mortality rate as indicators. These studies were designed to evaluate the epidemiology of esophageal cancer and examine the incidence, prevalence, and mortality due to cancers (13-16). The second group included studies concerning disability adjusted life years (DALYs), years of life lost (YLLs), and years lost due to disability (YLD) as health gap indicators. Unlike the first group studies, these studies are rare and have been conducted at regional levels (17, 18).

Esophageal cancer has put an extensive burden on the health, life expectancy, and well-being of Iranian population, especially in northern areas. Moreover, few studies have examined the burden of disease in the general population. Therefore, the present study was conducted to report the burden of esophageal cancer in Iran during 1995-2015 by acquiring data from Global Burden of Disease (GBD). Furthermore, the aim of this study was to describe the burden of esophageal cancer via DALY approach, which has introduced GBD methods and is also helpful for health policy-makers. Cancer burden studies are potentially important in public health decision-making because they help detect improvements in information systems and cost-effectiveness studies.

Methods

Data were retrospectively collected from the Global Burden of Disease (GBD) during 1995-2015 and published by the Institute for Health Metrics and Evaluation (IHME). In the GBD, data are collected and analyzed by a consortium of more than 1800 researchers in more than 120 countries. Preliminary data included premature death and disability from more than 300 diseases and injuries in 20 groups separated by age and sex in 188 countries during 1990-2018. In GBD studies, a comprehensive database of death registration system, vital registration, verbal autopsy, mortality surveillance, and other sources is used to assess the outcomes of health loss, including deaths and death rates, YLLs, YLDs, and DALYs. A complete description of the data, statistical modeling, and metrics are explained in detail elsewhere (19-21).

To better characterize the burden of esophageal cancer

in Iran, we needed to collect reported death number and crude incidence and prevalence rate. The incidence rate refers to the number of new cases in a fixed time period divided by the number of people at risk. On the other hand, the prevalence rate is the number of people with the disease at a given time divided by the number of people at risk. DALY is a tool developed by the World Health Organization (WHO) to measure, compare, and analyze the burden of various diseases (22, 23). The DALY combines time lost through premature death and time lived in states of less than optimal health, generally referred to as disability. This metric contains 2 components: years of life lost due to premature mortality (YLLs) and number of years lost due to disability (YLDs). A DALY is equal to the loss of one year of healthy life from the combined impacts of mortality and disability (24, 25).

The YLLs for a cause are basically calculated through the number of cause-specific deaths in an age group multiplied by a standard life expectancy at which death occurs (26). The YLDs for a particular cause were calculated by multiplying the number of incident cases by the disability weight by the average duration of the case until remission or death. The weight of disability has been reported by the WHO studies for various diseases (27, 28).

Stata Version 13 and Excel 2016 were used to analyze data and report DALY numbers and its components based on gender and age group during 1995-2015. To assess statistical significance according to trend, the Cochran-Armitage test was applied. Also, t test was used to analyze gender groups, with significance level set at $p < 0.05$. The age groups were categorized according to the method proposed by WHO and other studies. These groups include younger than 5 years, 5-14 years, 15-49 years, 50-69 years, and older than 70 years (29).

Results

GBD results for esophageal cancer in Iran are presented here based on the following parameters: The disability-adjusted life years (DALYs), years of life lost due to premature mortality (YLLs), number of years lost due to disability (YLDs), death, incidence, and prevalence rate.

During 1995-2015, there were 13 144 deaths related to esophageal cancer in Iran. The number of deaths caused by esophageal cancer increased in Iran from 1853 in 1995 to 3261 in 2015 in both genders. **Table 1** demonstrates death number, incidence, and prevalence rate per 100 000 due to esophageal cancer in Iran.

DALYs and its component

The estimated esophageal cancer in Iran during 1995-2015 was 304 102 DALYs. **Table 2** demonstrates the

Table 1. The number of death, incidence, and prevalence rate of esophageal cancer in Iran during 1995- 2015

Years	Death Number				Crude Incidence Per 100 000				Crude Prevalence Per 100 000			
	Male	Female	Both	p	Male	Female	Both	p	Male	Female	Both	p
1995	1099	754	1853	0.004	3.12	2.26	2.7	0.003	3.33	2.58	2.96	0.009
2000	1282	883	2165		3.49	2.57	3.04		4.02	3.28	3.66	
2005	1726	1187	2913		4.55	3.38	3.98		5.62	4.72	5.18	
2010	1775	1177	2952		4.69	3.3	4		6.14	4.93	5.54	
2015	2085	1176	3261		5.28	3.21	4.26		7.09	5.07	6.09	

P-value was statistically significant between male and female groups ($P < 0.05$); it was 0.004, 0.003, and 0.009 for death number, incidence rate, and prevalence rate, respectively.

Table 2. The death and DALYs number of esophageal cancer in different age groups in Iran during 1995- 2015

Age groups	DALYs Number and Rate						Death Number		
	Female		Male		Total	Female	Male	Total	
	Number	Crude Rate per 100,000	Number	Crude Rate per 100,000					
Younger than 5	0	00	0	00	0	00	0	0	0
5-14 years	0	00	0	00	0	00	0	0	0
15-49 years	31148	25.72	37587	29.06	68735	27.4	678	816	1494
50-69 years	66003	289.66	93301	397.38	159304	344.02	2409	3438	5847
>70 years	27389	496.8	48674	788.42	76063	649.62	2092	3711	5803
All ages	124540	56.93	179562	78.81	304102	68.02	5178	7966	13144

Table 3. YLLs and YLDs of esophageal cancer in different age groups in Iran during 1995-2015

Age	Year	YLLs		YLDs		DALYs		Both	Cochran-Armitage test Z= 1.8 P value= 0.072
		Female	Male	Female	Male	Female	Male		
15-49 years	1995	5209	5311	29	29	5238	5340	10578	
50-69 years	1995	10113	14181	84	117	10197	14298	24495	
>70 years	1995	3650	6156	53	86	3703	6242	9945	
All ages	1995	18970	25649	167	232	19137	25881	45018	
15-49 years	2000	6178	6481	40	40	6218	6521	12739	
50-69 years	2000	11211	15387	102	133	11313	15520	26833	
>70 years	2000	4484	7560	71	113	4555	7673	12228	
All ages	2000	21873	29427	213	287	22086	29714	51800	
15-49 years	2005	6966	8600	52	60	7018	8660	15680	
50-69 years	2005	14190	18549	139	167	14329	18716	33045	
>70 years	2005	6756	11169	113	178	6869	11347	18216	
All ages	2005	27912	38319	304	406	28216	38725	66941	
15-49 years	2010	6162	8185	49	61	6211	8246	14457	
50-69 years	2010	13891	18994	145	182	14036	19176	33212	
>70 years	2010	6658	11287	127	203	6785	11490	18275	
All ages	2010	26708	38466	321	447	27030	38914	65944	
15-49 years	2015	6408	8750	54	69	6462	8819	15281	
50-69 years	2015	15951	25346	177	245	16128	25591	41719	
>70 years	2015	5365	11701	112	221	5477	11922	17399	
All ages	2015	27724	45798	342	535	28066	46333	74399	

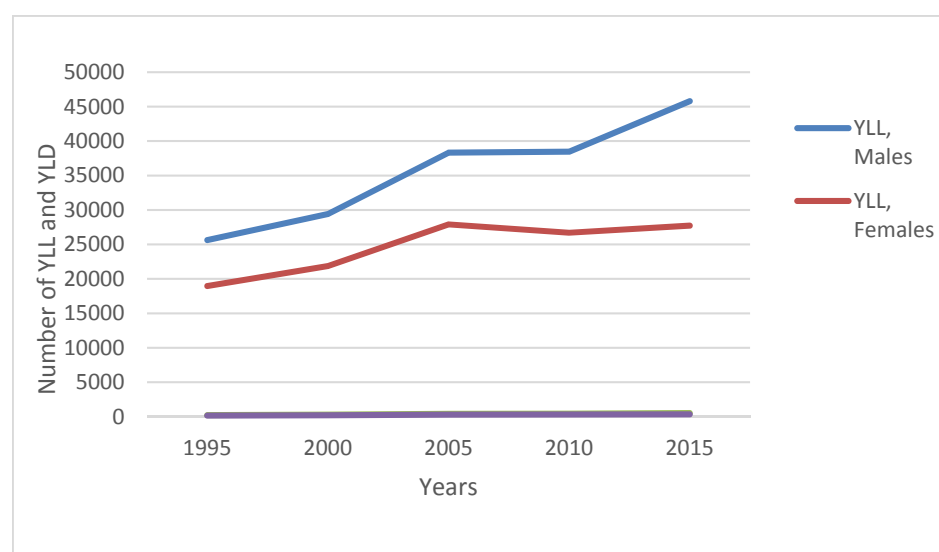
number of DALYs and death due to esophageal cancer in Iran during 1995- 2015 according to age groups. As presented in the table, 50-69 age group and over 70 years age group had the highest DALYs.

Table 3 and Fig. 1 present the number of DALYs, YLLs, and YLDs regarding esophageal cancer by age and gender in Iran during 1995-2015. In both genders and all ages, the number of DALYs indicates a significant increase from 45018 in 1995 to 74399 in 2015.

Data showed that YLLs are the main contributor to

DALY calculations for all ages and both genders. YLLs were 44619 in 1995 and 73522 in 2015, while they were 399 in 1995 and 877 in 2015. Furthermore, YLLs were higher than YLDs in all years and all group ages.

Our findings demonstrated that the burden of esophageal cancer was higher in males than in females. Also, the overall DALYs for all years and all ages were 179 562 for males and 124 540 for females (Table 2). As displayed in Fig. 2, the DALY rate per 100 000 esophageal cancer cases during 1995-2015 was higher for males than females.

**Fig. 1.** Sex differentials in burden of esophageal cancer by years in Iran during 1995-2015

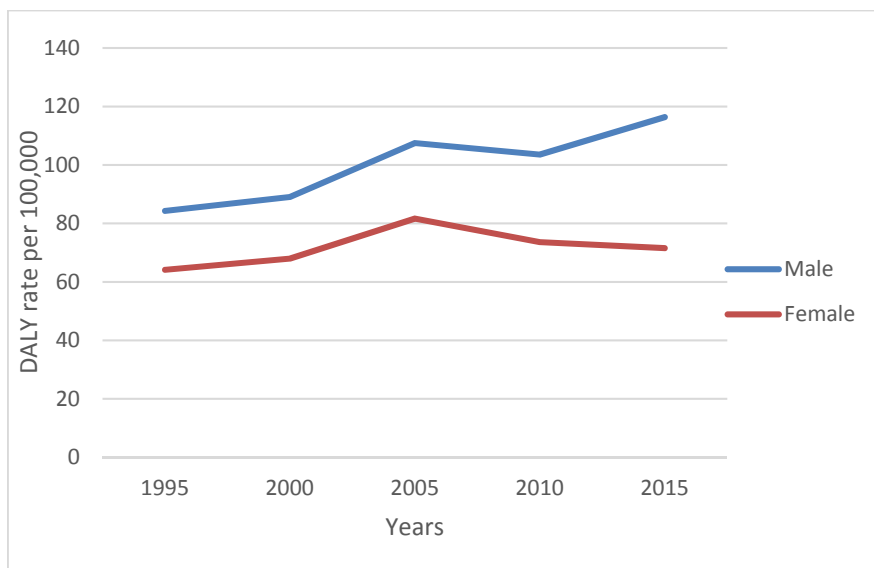


Fig. 2. DALY rate per 100 000 for esophageal cancer by sex during 1995-2015 in Iran

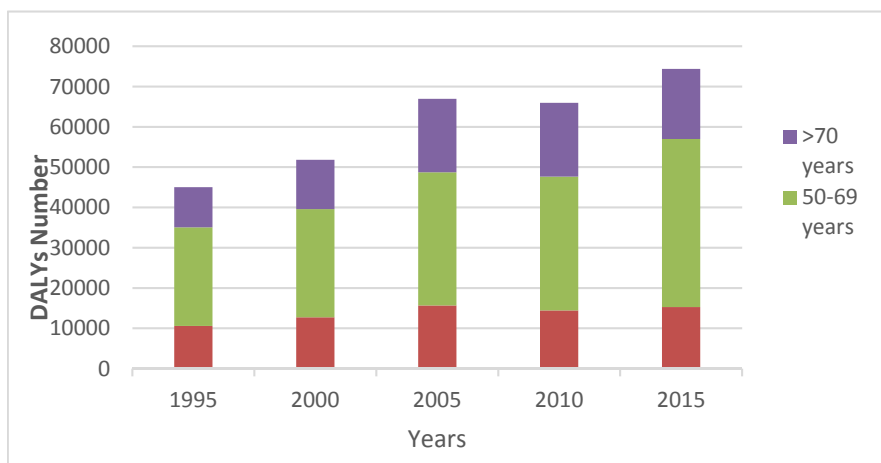


Fig. 3. DALYs number of esophageal cancer in different age groups by years in Iran during 1995-2015

In all age groups, the burden of esophageal cancer was higher in males than in females. Table 3 displays that in 2015 DALYs in all ages were 46333 for males and 28066 for females.

The results of this study indicated that the maximum of DALYs during 1995-2015 was associated with the 50-69 age range for which DALY values were 24495 in 1995 and 41719 in 2015. Figure 3 displays the DALYs for different age groups. As demonstrated, in all years, the 50-69 age groups had the highest DALY due to esophageal cancer in Iran. Furthermore, Table 3 displays the number of DALYs according to sex and age groups. For both genders and all years, the DALYs were higher in 50- 69 age groups than other groups.

Discussion

The present study was based on GBD findings from 1995 to 2015 for all ages and both genders. Moreover, this study was the first comprehensive effort to report the burden of esophageal cancer in Iran at the general population level.

About 13144 deaths and 304 102 DALYs attributed to esophageal cancer were estimated during 1995-2015 in

Iran. The present study clearly showed that DALYs, epidemiological indicators, the number of deaths, and incidence, and prevalence rate of this cancer increased significantly in both genders and all ages in Iran during the period studied. Furthermore, the number of DALYs due to esophageal cancer for both genders was 45 018 by all ages in 1995 and 74 399 in 2015. Incidence rate per 100 000 was 2.7 and 4.26 in 1995 and 2015, respectively. Prevalence rate increased from 2.96 to 6.09 per 100 000 during 1995-2015. These findings are consistent with other reports and studies. Darabi et al. estimated that the incidence rate of esophageal cancer increased from 3.25 and 2.1 in 2001 to 5.57 and 5.62 per 100 000 in 2010 (13). Another study on the incidence cancer in Iran reported that age-standardized incidence rate per 100 000 for males increased from 4.64 to 5.83 during 2003 to 2006 (30). Notably, the burden of esophageal cancer is very high in some areas of Iran, particularly in northeastern parts located on Asian esophageal cancer belt. Regional studies indicate that the incidence and prevalence rate in the mentioned area is higher than other regions and national average. Some studies have shown that the age-standardized incidence rate was more than 43.3 and 36.3

per 100 000 in males and females, respectively, in the Golestan Province in the north of Iran (9, 31).

In line with previous studies, our results indicate that YLL is the main contributor to DALY calculations, as esophageal cancer is a mortal disease. In fact, the burden of fatal diseases predominantly affects premature death. This result is consistent with other studies. For instance, in a study conducted by Sun et al. in China, it was reported that YLLs contributed to 90% of the DALYs for esophageal cancer (32). Another study reported that YLL contributed to more than 90% of DALY rate for esophageal cancer in all people (33). Gonzalez-Leon et al. estimated the burden of diseases in Mexico in 2010 and reported that YLL and YLD for esophageal cancer were 6032 and 690, respectively (34).

Our findings also revealed that the burden of esophageal cancer was higher in males than in females for all age groups. During 1995-2015, the number of deaths was 7967 and 5177 for males and females, respectively, and DALYs number was 179 562 for males and 124 540 for females. Moreover, DALY rate related to esophageal cancer was higher in males than in females during 1995-2015 (Fig. 2). Examinations of the DALYs number based on gender and age group (Table 3) revealed that the number of DALY was higher in males than in females in all age groups. Several studies have confirmed these results (35-37).

For some reason, the burden of esophageal cancer was higher in males. According to studies conducted in Iran, more than 90% of esophageal cancers related to squamous cell carcinoma and this subtype of esophageal cancer were associated with tobacco and alcohol consumption, hot food and beverage, ingestion of N-nitroso compounds, smoking, and chewing nass (chewing tobacco mixture). Various studies in Iran have shown that these risk factors are less in females (16, 38-40). Moreover, the DALY rate per 100 000 during 2005-2015 decreased in females due to several reasons. The death number due to esophageal cancer has increased in females during 1995-2005, but it declined after 2005. Also, the incidence rate shows the same trend (Table 1). In addition, this decline could be due to changes in population structure and the mean age of females, which was less than that of males during the past years. This study showed that 35% of the changes in esophageal cancer burden during 1990-2013 can be due to population growth and 35.6% may be due to change in age structure (41).

The acquired data indicated that the 50-69 age group had a higher burden of disease than other groups in Iran during 1995-2015. The DALYs number for this group was 24 495 and 41 719 in 1995 and 2015, respectively. Number of DALYs was 0 for younger than 14 age group in all years. A study in China reported that patients aged 40 to 80 years account for more than 90% of total esophageal cancer DALYs (32). Studies in Iran have shown that the highest incidence of esophageal cancer is in the sixth decade of life (42-44).

There were some limitations in this study. First, GBD study does not distinguish between the burden of esophageal cancer due to adenocarcinoma of the esophagus and

esophageal squamous cell carcinoma. This could be a subject for future studies, as each of these burdens has its own burden of disease. Second, the estimates of GBD study depend on the quality and quantity of the available data sources because of the lag time for data reporting. The burden of cancers could not be estimated for countries that do not have a comprehensive system for registering and reporting cancers. For example, studies have shown that incidence and prevalence of esophageal cancer were much higher than estimates of GBD study in some regions of Iran (9, 45).

Conclusion

Esophageal cancer is still a public health problem in Iran. The majority of DALYs were due to years of life lost (YLL), suggesting the need for prevention, early detection, and screening programs. Since the findings of this study and those of others have shown that the burden of esophageal cancer is greater in the 50-69 age group and given that the young Iranian population is approaching the at-risk age group, policymakers should evaluate the future tasks among different health care sections by considering prevention, early detection, approaching, and rehabilitation.

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Conflict of Interests

The authors declare that they have no competing interests.

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