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Burden of Esophageal Cancer According to World Health Organization Regions: Review of Findings from the Global Burden of Disease Study 2015

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Abstract

Background: Esophageal carcinoma is regarded as a malignant disease with fatal consequences. In cancers, it was the sixth cause of death in the world, with an estimated 439025 deaths in 2015.
Objectives: We conducted a research to evaluate the esophageal carcinoma burden based on the World Health Organization regions, during 2000 to 2015.
Methods: Global Burden of Disease (GBD) was used to retrospectively collect the data from 2000 to 2015. The Institute for Health Metrics and Evaluation publishes the data. We utilized disability adjusted life years (DALY), incidence rate and prevalence rate to describe the esophageal cancer burden in the world.
Results: In 2015, there were a total of 9854406 DALYs attributed to esophageal cancer where the majority were related the years of life lost (YLL) (9725791), and 128613 of the total were concerned with years lost due to disability (YLD). The highest of DALYs was in the Western Pacific region with 4773660 of the total. The Eastern Mediterranean region, with 516412 DALYs, shows the lowest number.
Conclusions: The esophageal carcinoma is still a public health problem in high incidence countries. In all countries, the majority of the DALYs is related to YLL, indicating that prevention and early detection should be taken seriously. The burden of esophageal cancer is different in geographical regions. Therefore, a suitable and specific program in every region and country should be developed.

Keywords: Esophageal Neoplasms, World Health Organization, Global Burden of Disease

1. Background

Esophageal carcinoma is considered as a malignant disease with deadly consequences in developed and developing countries (1, 2). Between cancers, it is the sixth cause of death in the world, with an estimated 439025 deaths in 2015 (3, 4).

The burden of esophageal cancer widely varies across the world, with a disability adjusted life years (DALYs) of 516412 in Eastern Mediterranean and 4773660 in Western Pacific regions (4). In 2012, age-standardized incidence rate (ASR) of esophageal cancer was 0.8 per 100.000 people for men in Western Africa, 13.7 in Southern Africa and 17 in Eastern Asia (3). Although the incidence rate of the esophageal cancer is high, the survival rate is low in patients suffering from this disease. The survival rate of esophageal cancer has remained low over the last decades, especially in developing countries. Studies have shown that the 5-year survival rate is less than 20% in men. For instance, Harirchi et al. showed that it was less than 15% in Iran (5-7).

Studies concerned with the burden of cancers are used to measure the progress of the health sector, providing a comprehensive assessment of incidence, mortality, and disability for all the cancers. Furthermore, it determines the priorities for interventions and decisions (8).

According to literature, studies calculating the burden of esophageal cancer are classified into two groups. The first group is related to the epidemiology of esophageal cancer, including, number of deaths, prevalence, incidence, and mortality rate (9-11).

The other group is linked to studying the morbidity of esophageal cancer. These studies calculate the total time lost concerning premature death and disability. The DALY, years of life lost (YLL) and years lived with disability (YLD) is applied in these researches (8, 12, 13).

2. Objectives

In this research, we present a study to assess the burden of the esophageal cancer based on the World Health Organization regions, during 2000 to 2015. Moreover, we applied the DALY indicator to describe the esophageal cancer burden, using the Global Burden of Disease (GBD) methods. This study would be helpful for health policy makers in countries located in the esophageal cancer belt, such as the Islamic Republic of Iran, since the studies of cancer burden help to evaluate the budgetary impacts of health plans and provide a background for designing cost-effectiveness studies.

3. Methods

Global Burden of Disease (GBD) was used to retrospectively collect the data, from 2000 to 2015. The Institute for Health Metrics and Evaluation (IHME) publishes the GBD studies. In the GBD research, the primary data are number of deaths and disabilities. These data are collected and reported based on age groups and sex, for more than 350 disease and injuries. Moreover, the GBD provides a tool to quantify health loss, these instruments include death numbers, mortality rates, YLLs, YLDs, and DALYs. Various sources are used to calculate the morbidity and mortality indicator, including, the registration of the vital event, verbal autopsy, surveillance of the maternal and child death, and other sources. A detailed description of methods of the GBD study has been published in the references (14-16).

For the estimation of esophageal cancer burden we applied the DALY indicator. It was first designed by the World Health Organization (WHO) to compute and evaluate the burden of diseases (17, 18). This measure mixes the years of life lost and years lived with disability for a special cause. The DALY is obtained by summing YLLs and YLDs for each sex and age group in a given year. In general, a DALY is equivalent to losing one year of healthy life extracted from the combination of mortality and morbidity (19, 20).

The YLLs measure the lost years of life due to deaths, therefore for a given cause, age, and sex, this metric is equal to the death number multiplied by the standard life expectancy (17). The YLD measures the disability due to a specific cause in a particular time period. It is determined by multiplying the incidence number for a specific reason by the duration of disability and a weight factor (21).

To estimate the esophageal cancer burden in the world, we have linked the DALYs related to the cancer of esophagus based on the World Health Organization regions. We have carried out the following steps.

First, we divided countries according to the WHO regions. The burden of esophageal cancer was obtained by the GBD 2015, including incidence rate, prevalence rate, number of death and DALY. The WHO regions include the Western Pacific, Eastern Mediterranean, European, South East Asia, Pan American and African region. Second, to get a view of the burden of the disease, we selected 5 top countries with a high value of DALY in each region of the WHO. Third, we compared the burden of the esophageal cancer in WHO regions and 5 top countries with a high value of DALY. For a more detailed study, the burden of esophageal cancer was surveyed during 2000 to 2015.

In this study, we report the burden of esophageal cancer using age groups and sex. The age groups are under 14 years, 15 - 49 years, 50 - 69 years and > 70 years. Furthermore, we depicted the esophageal cancer burden based on YLL and YLD. We used the STATA package, version 13 for our analysis.

4. Results

4.1. Incidence, Prevalence and Death

In 2015, there were 439025 global deaths caused by esophageal cancer where the global incidence and global prevalence rate were 6.54 and 10.12 per 100.000 people, respectively. Table 1 displays the death number, rate of incidence and prevalence for esophageal carcinoma, relative to the world areas. The Western Pacific with a death number of 225672 (more than 50%) is ranked first, and the Eastern Mediterranean area with a death number of 1774 is at the end of the ranking. The incidence and prevalence rate for the Western Pacific is more than 2 times of the global average. More than half of the deaths caused by esophageal cancer happened in China, having a death number of 202042. It is worth mentioning that Japan has the highest incidence (22.29 per 100.000) and prevalence rate (54.62 per 100.000).

4.2. DALY

In 2015, there were a total of 9854406 DALYs attributed to esophageal cancer, where the majority were related to the years of life lost (YLL) (9725791), and 128613 of the total were concerned with years lost due to disability (YLD). The worldwide DALY value is 7331669 and 2022737 for men and women, respectively. The greatest burden of DALYs has happened in the Western Pacific (4773660). The Eastern

Table 1. The Death Number, the Rate of Incidence and Prevalence in Top Five Countries in the WHO Regions, in 2015.

Region and Country Name (Number of Deaths)	Incidence Rate per 100.000 People	Prevalence Rate per 100.000 People
Western Pacific (225672)	13.85	22.21
China (202042)	Japan (22.29)	Japan (54.62)
Japan (13717)	China (15.66)	China (23.42)
Vietnam 3791)	Mongolia (12.14)	New Zealand (17.80)
South Korea (2085)	New Zealand (8.66)	Mongolia (15)
Australia (1496)	Ausralia (7.83)	Ausralia (14.7)
Eastern Mediterranean (17741)	2.58	3.28
Pakistan (10253)	Afghanistan (1.69)	Pakistan (6.41)
Iran (3261)	United Arab Emirates (1.49)	Iran (6.09)
Afghanistan (673)	Morocco (1.22)	Djibouti (5.66)
Egypt (649)	Lebanon (1.19)	Somalia (3.85)
Somalia (546)	Yemen (0.97)	United Arab Emirates (2.66)
European (52584)	6.94	12.22
United Kingdom (8376)	Netherlands (18.02)	Netherlands (34)
Russia (7927)	United Kingdom (14.64)	France (26.38)
Germany (5884)	France (12.68)	United Kingdom (24.20)
France (5526)	Belgium (9.71)	Hungary (20.6)
Italy (2379)	Ireland (9.43)	Belgium (19.3)
South East Asia (66628)	3.40	4.48
India (49158)	North Korea (12)	North Korea (1595)
Indonesia (4981)	Thailand (5.43)	Thailand (8.30)
Bangladesh (3488)	Sri Lanka (4.39)	Sri Lanka (6.59)
Thailand (3330)	India (3.67)	India (4.78)
North Korea (3040)	Bangladesh (2.05)	Indonesia (2.65)
Pan American (40114)	4.66	7.68
United States (17588)	Uruguay (11.01)	Cuba (16.33)
Brazil (10895)	Cuba (8.99)	Uruguay (15.49)
Argentina (2581)	Barbados (8.54)	Barbados (15.44)
Canada (2198)	Canada (6.97)	Puerto Rico (14.18)
Mexico (1355)	Puerto Rico (6.87)	United States (11.92)
African (33844)	2.98	3.15
South Africa (5238)	Malawi (10.42)	South Africa (12.6)
Ethiopia (4090)	South Africa (9.64)	Seychelles (11.64)
Nigeria (2564)	Lesotho (9.4)	Botswan (10.62)
Uganda (2403)	Swaziland (9.15)	Malawi (10.32)
Democratic Republic of the Congo (2230)	Botswana (8.97)	Swaziland (10.06)
Global (439025)	6.54	10.12

Mediterranean region with 516412 DALYs showed the lowest number. Table 2 indicates the number of DALYs due to esophageal cancer, according to the WHO areas.

Table 3 shows the DALY number, according to the age group. In all the regions and countries, the highest burden is related to the age group of 50 - 69 years.

Figure 1 shows the trend of DALYs regarding esophageal cancer in the world, from 2000 to 2015, classified by the WHO areas. The findings indicated that the burden of esophageal cancer has had little change, from 2000 to 2015, of which the peak was more than 10 million DALYs in 2005. The majority of DALYs are distributed in the Western Pacific, in all the years.

Figure 2 shows the number of DALYs for top five countries, during 2000 to 2015. In all the years, China showed the highest value, but its trend has significantly declined.

Table 2. The Number DALYs Reported for the Top Five Countries in each WHO Region, in 2015

Region and Country Name	YLL		YLD		DALY		
	Male	Female	Male	Female	Male	Female	Total
Western Pacific region	3677664	1027312	51673	17010	3729338	1044323	4773660
China	3322076	943618	41970	14659	3364047	958278	4322325
Japan	201045	30061	7394	1441	208440	31502	239942
Vietnam	59113	24508	637	367	59751	24875	84626
Australia	19477	5750	336	198	19814	5948	25762
Malaysia	7180	3648	93	50	7274	3699	10973
Eastern Mediterranean	262788	249284	2258	2080	265046	251365	516412
Pakistan	150359	173075	1138	1335	151498	174410	325909
Iran	45798	27724	535	341	46333	28066	74399
Afghanistan	7347	12905	52	83	7399	12989	20388
Egypt	12339	5698	113	55	12452	5753	18206
Somalia	8351	6298	58	44	8409	6343	14753
European region	863209	217066	13332	4627	876542	221694	1098236
Russia	154069	28015	1805	539	155874	28554	184428
United Kingdom	101874	38887	1588	917	103463	39805	143268
Germany	95068	22556	1722	489	96791	23046	119837
France	93752	16067	1893	517	95646	16585	112231
Ukraine	43866	3833	731	103	44597	3937	48535
Southeast Asia region	1093639	568920	10685	6376	1104324	575297	1679621
India	800183	440550	7622	4801	807805	445352	1253157
Indonesia	75056	52155	770	590	75827	52746	128573
Bangladesh	70935	13364	683	156	71619	13520	85140
Thailand	54170	18244	704	297	54875	18542	73417
North Korea	48652	23948	476	295	49129	24243	73373
Pan American region	678533	158791	9555	3061	688088	161852	849940
United States	299982	58317	4738	1314	304720	59631	364352
Brazil	208744	48126	2401	757	211146	48884	260031
Argentina	36603	11722	491	231	37094	11954	49048
Canada	33844	7365	515	168	34359	7533	41893
Mexico	21029	7137	293	116	21323	7253	28576
African region	611934	258727	4783	2297	616717	261025	877743
South Africa	84280	36172	819	448	85100	36620	121720
Ethiopia	62446	38777	481	330	62927	39107	102035
Nigeria	57769	12705	506	127	58276	12832	71109
Uganda	43048	20223	306	161	43354	20384	63739
Malawi	43401	18586	283	133	43685	18719	62405
Global	7238663	2487128	93005	35608	7331669	2522737	9854406

Other countries have an increasing trend during 2000 to 2015.

Figure 3 shows the DALY rate per 100.000 people in the top five countries. The same as the number of DALYs, in all the years, China has the highest DALY rate, but its trend has significantly diminished. India has the second rank in the DALY number, but it is at the bottom of the rank in the DALY rate.

5. Discussion

In this study, we have provided a comprehensive report on the burden of esophageal cancer, based on the WHO areas. The reports indicated that the trend of the esophageal cancer burden has increased by 2005. Then, it has diminished. In addition, the pattern for the esophageal cancer burden, based on geographical distribution, has been investigated.

Table 3. The Number DALYs Reported According to the Age Group for the Top Five Countries in each WHO Region, in 2015

Region and Country Name	Age Groups			
	Under 14	15 - 49 years	50 - 69 years	70+ years
Western Pacific region	0	508610	3014182	1308584
China	0	463375	2775655	1159027
Japan	0	9135	119469	93140
Vietnam	0	18494	46759	18750
Australia	0	2440	14393	9739
Malaysia	0	1739	5649	2787
Eastern Mediterranean	0	133195	187088	50964
Pakistan	0	92866	107810	21834
Iran	0	10103	26615	13613
Afghanistan	0	5271	7262	1902
Egypt	0	8681	16868	3473
Somalia	0	2551	5470	1705
European region	0	117812	663746	285485
Russia	0	17696	129834	33087
United Kingdom	0	11636	76063	60461
Germany	0	10215	67888	36519
France	0	8766	65099	27813
Ukraine	0	6037	34330	6914
Southeast Asia region	0	378926	726381	219207
India	0	287922	549866	156293
Indonesia	0	16083	23542	6457
Bangladesh	0	27312	23261	10155
Thailand	0	14874	39314	12395
North Korea	0	14240	47177	20290
Pan American region	0	114993	503653	216483
United States	0	36414	230041	102296
Brazil	0	47509	155122	45757
Argentina	0	5282	25506	15767
Canada	0	3876	25720	13272
Mexico	0	6395	14490	7209
African region	0	176148	361558	120557
South Africa	0	19245	65756	18472
Ethiopia	0	17207	28077	14201
Nigeria	0	13652	28297	7664
Uganda	0	14807	31128	9848
Malawi	0	21492	27740	8924
Global	0	1444592	5494240	2211606

About 439025 deaths and 9854406 DALYs of esophageal cancer happened in 2015. The global incidence and prevalence rates were 6.54 and 10.12 per 100.000, respectively. In 2015, according to the WHO regions, the Western Pacific area with more than 50% of the number of deaths (225672) and DALYs (4773660), compared to other regions, ranked first in the esophageal cancer burden. The Mediterranean region with a death number of 17741 and DALY of 516412 was indicated as the last rank.

Moreover, in 2015, the results showed that the incidence and prevalence rates of the esophageal cancer in the Western Pacific region were 13.85 and 22.21 per 100.000 people, respectively, almost twice the global average. In this area, Japan and China led to the highest incidence, prevalence and number of death. In Japan, incidence and prevalence rates are reported 22.29 and 54.62, respectively.

Mainly, China and Japan have caused the increased burden of esophageal cancer in the Pacific region. Esophageal

cancer has always been a serious issue in these countries. In 2008, a study showed that esophageal cancer has led to 11746 and 211084 deaths in Japan and China, respectively (22).

The current study clearly demonstrated that the DALYs related to esophageal cancer in men (7331669) are higher than in women (2522737). However, there are two countries (Afghanistan and Pakistan) that their DALYs are higher among women. A study in Brazil estimated that the total DALYs of esophageal cancer was 3235 for men, and it was 918 for women (23). Another study in China reported that, per 100.000 people, the incidence rate of esophageal cancer was 10.39 in men, and it was 7.44 in women (24). In addition, a study showed that the incident cases of the esophageal cancer for men and women were 483000 and 352000, respectively (8). There is also a study indicating that the DALY rate of esophageal cancer for women is higher, in comparison with those in men (25).

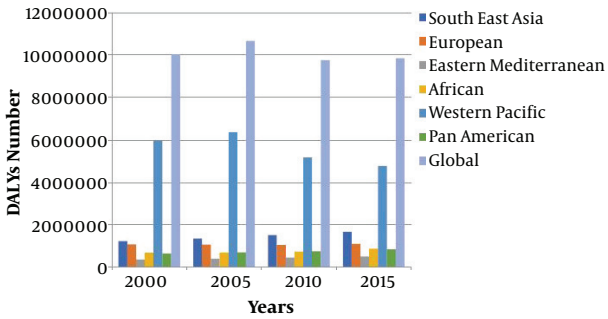

Figure 1. DALYs number of esophageal cancer in WHO regions, 2000 to 2015

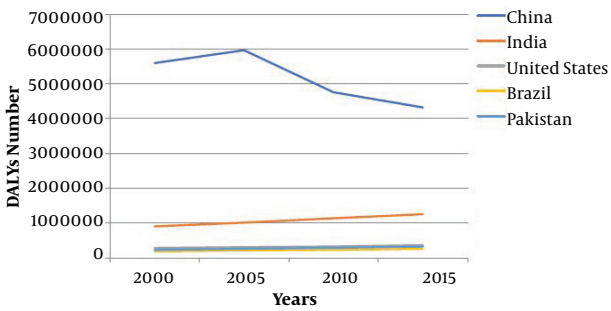

Figure 2. DALYs number due to esophageal cancer for top five countries, 2000 to 2015.

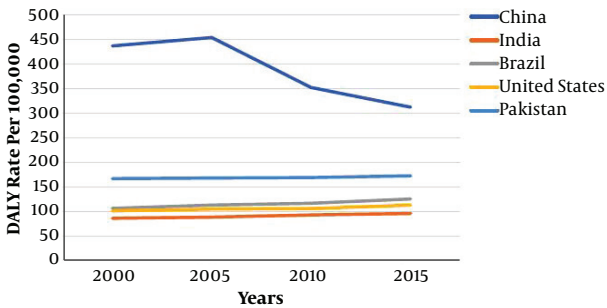

Figure 3. DALY rate per 100.000 for top five countries, 2000 to 2015

In this study, the greatest cancer burden of the esophagus is related to the age group of 50 - 69 years, in all the WHO regions and countries. In some countries, however, the burden of esophageal cancer, in the age group of 15 to 49 years, is higher than the age group of < 70 years. For example, in the region of the Africa, the DALY number was 176148 and 120557 for the age groups of 15 - 49 and < 70 years, respectively. This finding suggests that the risk factors of esophageal cancer are different in the world. It is very important to consider that the burden of esophageal cancer varies depending on lifestyle, the factor of genetics and environmental effect (26, 27).

Our research, like the results of previous studies, displays that the YLLs are a major part of DALYs calculation for esophageal carcinoma burden. It is presented that esophageal carcinoma has a high mortality. In China, the research found that more than 90% of the DALY for esophageal carcinoma were due to premature death (28). Jayatilleke et al. have reported that YLL contributed to the majority of the DALY rate (90%) for esophageal carcinoma, in all ages (29). Another study, in 2010, estimating the burden of diseases between Mexican people, reported that YLL and YLD were 6032 and 690, for esophageal cancer, respectively (12).

For more careful study on the burden of esophageal cancer, we assessed the DALY, in 2000 to 2015. Globally, DALYs were 1023116 in 2000, gained the peak of 10665358 in 2005. Then, decreased by 2015. Regionally, the Western Pacific area always has the highest DALY, in all the years, where DALYs were 5968131 and 4773660, in 2000 and 2015, respectively. The lowest DALYs happened in the Mediterranean area during these years. Internationally, in 2015, the top 5 countries which had the highest esophageal cancer DALYs were China, India, United States, Pakistan and Brazil. The following points should be noted when one wants to review the esophageal cancer burden in the 5 top countries and WHO areas. Firstly, although the Western Pacific area always had the highest DALYs related to esophageal cancer, the trend of DALY has been decreasing in this area. In addition, China is located in the Western Pacific area, and it has more than half of the global DALYs.

Secondly, China had the highest DALYs during 2000 to 2015 whereas the trend of esophageal cancer DALYs has been decreasing. On the other hand, it has been increasing

in other countries.

These findings further support the idea of which countries of Asia are also located on the esophageal cancer belt. This area expands from Northern China through Southern Russia, Northern Afghanistan and North-Eastern Iran to Eastern Turkey (30). All the countries located at the esophageal cancer belt, except Turkey, have a high burden of the esophageal cancer in our study.

Interpretation of the results based on the geographical area shows a series of homogeneous and heterogeneous patterns associated with the burden of the esophageal cancer. First, in all the areas and countries, age and sex are important factors for the esophageal burden. Second, in all the geographical areas, the burden of esophageal cancer is more related to YLL. Third, the African region and its countries have a special pattern. In the countries of this region, the burden of the esophagus in the age group of 15 - 49 years is more than the age group of > 70 years.

Despite the fact that the GBD study is effective in estimating the global burden of diseases, it has some critical limitations. It does not distinguish between the esophageal cancer burden by its subtype. This could be a topic for upcoming studies since each has its own burden of disease. Moreover, adenocarcinoma of the esophagus is more common in developed countries, particularly the United States (31). In developing countries, the squamous cell carcinoma of esophageal is more common (32).

The assessment of GBD study is contingent on the accessibility of data sources due to the delay time for data reporting. It may result in a miscalculated cancer burden for countries where there does not exist a complete system to register and report the cancers. For instance, studies have revealed that in some regions of Iran, the rate of incidence and prevalence for esophageal cancer are much higher than estimations conducted in GBD study (33, 34).

5.1. Conclusions

Esophageal cancer is still a public health issue in the world. In all counties, the majority of DALYs were related to YLL, indicating that prevention and early detection should be seriously considered. Regionally, the burden of disease is different according to the WHO regions. Therefore, a specific and suitable program should be used in every region and country. In addition, the burden of esophageal cancer is more about the elderly people, suggesting that health policy makers pay more attention to programs related to health of the elderly people, especially in developing countries.

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Footnotes

Authors' Contribution: Ahmad Faramarzi and Mohammad Arab developed the research idea. Azin Nahvijou conducted the analyses, supported by Seyed Yaser Hashemi and Javad Javan-Noughabi. All authors interpreted the findings. Ahmad Faramarzi and Azin Nahvijou wrote the manuscript. All authors commented on and approved the manuscript.

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