

# Global Incidence and Mortality of Esophageal Cancer and Its Relationship with the Human Development Index (HDI); An Ecology Study

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## Abstract

**Background and objective:** The esophageal cancer was considered as the eighth common type of cancer as well as the sixth cause of mortality across the world according to the report of International Agency of Research. The current study was aimed to evaluate the epidemiology, incidence, and mortality rates of esophageal cancer in Iran compared to other regions of the world. **Methods and materials:** This study was an ecologic study in Asia for assessment of the correlation between age-specific incidence rate and age-specific mortality rate (ASMR) with HDI (life expectancy at birth, mean years of schooling and gross national income (GNI) per capita) Data about SIR and SMR for every Asian country for the year 2012 were obtained from the global cancer project. The bivariate and regression tests were used to evaluate the correlation between the incidence and mortality with HDI. The statistical analysis was carried out by Stata-14 and the significance level was estimated at the level of 0.05. **Results:** Esophageal cancer is the eighth most common cancer worldwide, with an estimated 456,000 new cases in 2012 (3.2% of the total). A significantly negative correlation was found between the incidence and mortality rates with HDI and esophageal cancer ( $r = -0.158$ ,  $P < 0.05$ ;  $r = -0.219$ ,  $P < 0.05$ ). The linear regression indicated the decreased incidence and mortality rates by increasing HDI, MYS, and GNI. This amount was not statistically significant ( $P > 0.05$ ). However, increased LBE would decrease the incidence and mortality rates of esophageal cancer ( $B = -0.11$ , and  $B = -0.12$ ). **Conclusion:** The incidence and mortality rates of esophageal cancer in the developing countries are higher than developed countries. A correlation was indicated between the incidence and mortality rates of esophageal cancer with HDI and life's expectancy hindering the need for decreasing risk factors of esophageal cancer in the developing countries.

**Keywords:** Linear regression- updated esophageal cancer- Human Development Index- Ecological Study, in the world

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## Introduction

The reports indicated that some 45% of the mortality rate in the world would be related to noncontagious diseases in the years conducted to 2015. The cancers were demonstrated as the most important noncontagious diseases burdening a heavy load on the society. In other

hand, the relative controlling of contagious diseases, increasing life expectancy, life style change, increasing the environmental risk factors, genetic property, and aging were reported as the risk factors of this disease in the recent and future decades [1-5]. Despite the high rate of cancers mortality, it is estimated that more than one-third of the diseases would be preventable and the

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remainders treatable potentially provided with on time and early diagnosis [6].

The esophageal cancer was considered as the eighth common type of cancer in the world with a low survival rate among other types of cancer. Several studies reported the significant incidence rate of this cancer in the recent decades [7].

Esophageal cancer was defined as cancerous tissue growth in esophagus in which the cells are being divided without controlling. This type of cancer is common in Asia, Northern Iran (Gorgan, Torkman Sahra), beyond China, Asian Republicans of the Soviet Union [7-8]

The prevalence of the disease in some regions of Asia from Northern provinces of China to Caspian banks in Iran was estimated as 100 cases per 100000 people with a mortality rate of 20%. The aforementioned regions were known as esophageal cancer zone [9].

While most of the causes were reported unknown, smoking, drinking, and hot tea were indicated as the risk factors. Moreover, high consumption of kipper, salty nutrition such as salty cabbage, and cucumber, salty fish, mushrooms toxins, vitamin lacks, minerals, inorganic and chemical compounds and unknown factors were reported as the risk factors [10-14]. Dysphagia, heartburn, anorexia, weight loss, dysphonia, hidden gastrointestinal bleedings, pain, repetitious pulmonary infections were considered as the symptoms of the disease [9-10].

The current study was aimed to evaluate the epidemiology, incidence, and mortality rates of esophageal cancer in Iran compared to other regions in the world.

## Materials and Methods

Data about the incidence and mortality rate of LC for the year 2012 was obtained from the global cancer project for 172 countries (10). Data about the HDI and other indices were obtained for 169 countries from the United Nations development program (UNDP) data base[11].

**Estimation incidence:** The methods to estimate the gender- and age-specific incidence rates of cancer for a specific country fall into one of the following broad categories, in priority order: 1. Rates projected to 2012 (38 countries) 2. Most recent rates applied to 2012 population (20 countries) 3. Estimated from national mortality by modelling, using incidence mortality ratios derived from recorded data in country-specific cancer registries (13 countries) 4. Estimated from national mortality estimates by modelling, using incidence mortality ratios derived from recorded data in local cancer registries in neighboring countries (9 European countries) 5. Estimated from national mortality estimates using modelled survival (32 countries) 6. Estimated as the weighted average of the local rates (16 countries) 7. One cancer registry covering part of a country is used as representative of the country profile (11 countries) 8. Age/gender specific rates for "all cancers" were partitioned using data on relative frequency of different cancers (by age and gender) (12 countries) 9. The rates are those of neighboring countries or registries in the same area (33 countries).

### Estimation mortality

Depending of the degree of detail and accuracy of the national mortality data, six methods were utilized in the following order of priority: 1. Rates projected to 2012 (69 countries) 2. Most recent rates applied to 2012 population (26 countries) 3. Estimated as the weighted average of regional rates (1 country) 4. Estimated from national incidence estimates by modelling, using country-specific survival (2 countries) 5. Estimated from national incidence estimates using modelled survival (83 countries) 6. The rates are those of neighboring countries or registries in the same area (3 countries) [15].

### HDI

The HDI is a composite measure of indicators along three dimensions: life expectancy, educational attainment, and command over the resources needed for a decent living. All groups and regions have seen notable improvement in all HDI components, with faster progress in low and medium HDI countries. On this basis, the world is becoming less unequal. Nevertheless, national averages hide large variations in human experience. Wide disparities remain within countries of both the North and the South; income inequality within and between many countries has been rising [16-17].

### Statistical analysis

In this study, we used the correlation bivariate method for assessment of the correlation between the incidence and mortality rates of cancer and the HDI. We also used linear regression models for assessment of the HDI effect on cancer occurrence rates. The significance level of 0.05 was considered. Data were analyzed by Stata computer software version 12.

## Results

Esophageal cancer is the eighth most common cancer worldwide, with an estimated 456,000 new cases in 2012 (3.2% of the total), and the sixth most common cause of death from cancer with an estimated 400,000 deaths (4.9% of the total).

These figures include both adenocarcinoma and squamous cell carcinoma sub-types. Around 80% of

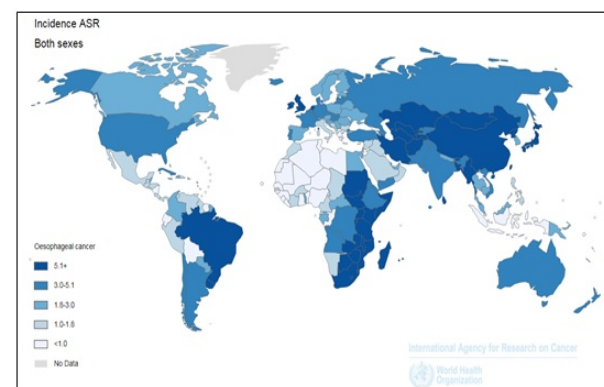


Figure 1. Distribution of the Standardized Incidence Rate of Esophageal Cancer in World at 2012 (Extracted from Globocan)

Table 1. Number, Crude, and Standardized Incidence and Mortality Rates of Esophageal Cancer in World in 2012

Countries	Incidence Rate			Mortality Rate			HDI
	Number	Crud rate	ASR(W)	Number	Crud rate	ASR(W)	
Very high human development							
Norway	233	0.8	2.5	200	1.9	2.0	0.942
Australia	1456	1.2	3.5	1277	2.9	2.9	0.933
Switzerland	603	1.4	3.8	434	2.7	2.6	0.934
Denmark	443	1.2	3.9	487	3.1	4.1	0.924
Germany	6950	1.4	4.0	5169	2.4	2.7	0.919
Ireland	424	2.0	5.7	361	4.3	4.7	0.902
United States	16968	1.1	3.2	15982	2.6	2.9	0.915
Canada	1837	1.0	2.8	1856	2.5	2.7	0.909
New Zealand	302	1.4	3.6	253	2.9	2.9	0.908
Singapore	137	0.9	1.7	126	1.8	1.6	0.92
Hong Kong, China (SAR)	223306	7.3	12.6	197472	9.0	10.9	0.907
Sweden	461	0.9	2.3	430	1.9	2.0	0.904
United Kingdom	8803	2.7	6.6	7929	5.0	5.6	0.899
Korea (Republic of)	2223	1.0	2.9	1551	1.9	1.9	0.891
Israel	140	0.5	1.2	118	1.1	1.0	0.891
Luxembourg	34	1.4	4.0	24	2.4	2.6	0.892
Japan	19683	2.8	6.1	12440	3.3	3.5	0.894
Belgium	969	1.5	4.6	721	2.4	3.2	0.889
France	4415	1.3	3.8	3826	2.5	2.9	0.887
Austria	447	1.1	2.8	351	1.7	2.1	0.887
Finland	282	1.0	2.4	240	2.1	1.9	0.887
Slovenia	84	0.7	2.1	79	1.3	1.9	0.878
Spain	2090	1.0	2.5	1728	1.7	1.9	0.874
Italy	1809	0.5	1.3	1746	1.0	1.2	0.876
Czech Republic	593	1.0	3.1	469	1.7	2.4	0.865
Greece	217	0.5	0.8	208	0.7	0.8	0.86
Estonia	54	0.9	2.2	67	1.9	2.6	0.856
Cyprus	17	0.5	1.0	14	1.0	0.7	0.849
Qatar	13	1.3	2.2	13	2.7	2.2	0.843
Slovakia	284	1.2	3.4	255	2.2	3.0	0.838
Poland	1506	1.0	2.2	1421	1.5	2.1	0.838
Lithuania	198	1.4	3.6	188	2.3	3.5	0.834
Malta	20	1.1	2.1	13	1.6	1.3	0.828
Saudi Arabia	25	1.3	1.4	210	2.3	1.3	0.83
Argentina	2263	2.0	4.0	1885	2.8	3.2	0.817
United Arab Emirates	40	1.4	2.0	39	3.1	2.0	0.829
Chile	798	2.0	3.2	695	2.8	2.7	0.831
Portugal	608	1.2	3.1	540	2.2	2.6	0.827
Hungary	603	1.2	3.6	539	1.8	3.1	0.824
Bahrain	10	1.1	1.7	6	1.7	0.9	0.815
Latvia	142	1.4	3.5	128	2.1	3.2	0.814
Croatia	243	1.1	2.8	219	1.6	2.5	0.817
Kuwait	11	0.7	0.8	15	1.9	1.0	0.796
Montenegro	17	0.8	1.8	19	1.4	1.9	0.799
High human development							
Belarus	451	1.4	3.0	410	2.2	2.7	0.796
Russian Federation	7263	1.6	3.1	6499	2.2	2.7	0.799
Oman	21	1.4	1.5	21	2.4	1.5	0.796
Romania	768	1.0	2.3	712	1.5	2.1	0.794
Uruguay	317	2.5	5.4	320	3.7	5.2	0.788

Continued Table 1. Number, Crude, and Standardized Incidence and Mortality Rates of Esophageal Cancer in World in 2012

Countries	Incidence Rate			Mortality Rate			HDI
	Number	Crud rate	ASR (W)	Number	Crud rate	ASR (W)	
Bahamas	6	0.7	1.5	6	1.5	1.5	0.79
Kazakhstan	1684	4.2	10.1	1555	6.5	9.3	0.782
Barbados	10	0.9	1.8	10	1.9	1.8	0.792
Bulgaria	222	0.7	1.6	183	1.0	1.3	0.781
Panama	55	1.0	1.5	53	1.8	1.4	0.733
Malaysia	483	1.3	2.0	328	1.5	1.4	0.779
Mauritius	50	1.9	3.3	50	3.3	3.3	0.765
Serbia	380	0.9	2.4	361	1.4	2.2	0.766
Cuba	834	2.1	4.6	735	3.0	4.0	0.773
Lebanon	34	0.4	0.7	34	0.7	0.7	0.766
Costa Rica	63	0.7	1.2	55	1.3	1.0	0.762
Iran (Islamic Republic of)	343	6.3	8.6	4915	9.2	7.8	0.769
Venezuela (Bolivarian Republic of)	336	0.8	1.3	313	1.3	1.2	0.77
Turkey	2536	1.7	3.5	2340	2.5	3.3	0.754
Sri Lanka	1407	5.9	5.6	1302	9.3	5.1	0.757
Mexico	1143	0.8	1.0	1055	1.3	0.9	0.753
Brazil	12907	2.9	6.1	9811	4.4	4.6	0.734
Georgia	48	0.4	0.6	45	0.6	0.6	0.755
Azerbaijan	440	3.2	4.6	404	4.5	4.2	0.745
Jordan	967	15.1	25.6	583	15.4	15.5	0.737
Ukraine	1897	1.3	2.5	1469	1.7	2.0	0.744
Algeria	169	0.4	0.6	157	0.7	0.5	0.737
Peru	336	0.8	1.2	311	1.2	1.1	0.731
Albania	51	0.7	1.2	55	1.2	1.3	0.759
Armenia	60	0.6	1.3	58	0.9	1.2	0.736
Bosnia and Herzegovina	73	0.7	1.1	94	1.4	1.2	0.735
Ecuador	144	0.6	1.0	129	0.9	0.9	0.725
China	223306	7.3	12.6	197472	9.0	10.9	0.713
Fiji	12	1.1	1.5	13	2.0	1.8	0.719
Mongolia	10	4.5	4.3	10	7.8	4.3	0.72
Thailand	2308	1.9	2.5	2061	2.4	2.2	0.733
Dominica	135	0.9	1.4	126	1.4	1.3	0.721
Libya	42	0.7	0.9	39	1.1	0.9	0.735
Tunisia	58	0.5	0.5	55	0.7	0.5	0.72
Colombia	846	1.2	1.9	754	2.0	1.7	0.712
Jamaica	66	1.1	2.2	63	1.9	2.1	0.727
Belize	6	1.7	2.8	6	2.8	2.8	0.706
Dominican Republic	135	0.9	1.4	126	1.4	1.3	0.709
Suriname	5	0.6	0.8	5	1.0	0.8	0.719
Maldives	10	4.5	4.3	10	7.8	4.3	0.683
Samoa	1	0.7	0.6	1	1.2	0.6	0.7
Medium human development							
Botswana	123	7.5	9.2	112	10.9	8.5	0.693
Egypt	1450	1.3	2.1	1337	1.8	2.0	0.681
Turkmenistan	719	12.0	19.7	663	16.6	18.5	0.678
Gabon	25	2.4	2.3	24	3.9	2.2	0.678
Indonesia	2191	0.7	1.0	2023	1.0	0.9	0.677
Paraguay	152	1.9	2.9	141	2.8	2.7	0.679
Uzbekistan	1180	5.2	6.0	1094	7.3	5.6	0.681
Philippines	715	0.7	1.1	623	1.1	1.0	0.671

Continued Table 1. Number, Crude, and Standardized Incidence and Mortality Rates of Esophageal Cancer in World in 2012

Countries	Incidence Rate			Mortality Rate			HDI
	Number	Crud rate	ASR (W)	Number	Crud rate	ASR (W)	
El Salvador	86	1.0	1.3	80	1.3	1.1	0.675
Viet Nam	2763	2.2	.1	2577	2.7	2.9	0.668
Bolivia (Plurinational State of)	58	0.5	0.8	55	0.8	0.7	0.661
Kyrgyzstan	187	3.2	4.9	172	4.3	4.5	0.647
Iraq	190	0.7	1.2	176	1.0	1.1	0.659
Guyana	5	0.5	0.8	4	0.7	0.7	0.633
Nicaragua	32	0.6	0.9	29	0.8	0.8	0.63
Morocco	337	1.0	1.2	311	1.4	1.1	0.634
Namibia	18	1.3	1.3	18	2.2	1.3	0.625
Guatemala	154	1.2	1.6	143	1.4	1.5	0.611
Tajikistan	570	10.3	14.7	527	13.6	13.6	0.617
India	41774	4.1	4.1	38683	5.7	3.8	0.599
Honduras	64	0.9	1.2	62	1.2	1.2	0.614
Bhutan	32	6.9	5.7	31	8.2	5.5	0.589
Timor-Leste	10	0.9	1.7	10	1.3	1.7	0.62
Syrian Arab Republic	138	0.6	1.0	130	0.9	1.0	0.635
Vanuatu	0	0	0	0	0	0	0.591
Congo	18	0.8	0.8	16	1.1	0.7	0.576
Zambia	583	5.5	9.1	533	7.1	8.5	0.565
Ghana	89	0.6	0.5	72	0.7	0.4	0.57
Lao People's Democratic Republic	25	0.4	0.6	25	0.5	0.6	0.563
Bangladesh	13909	11.3	12.7	12909	14.1	11.8	0.565
Cambodia	237	1.6	2.4	222	2.0	2.3	0.546
Low human development							
Kenya	3432	8.4	17.6	3120	11.0	16.5	0.541
Nepal	504	2.7	2.5	466	3.3	2.3	0.545
Pakistan	5168	3.5	4.1	4748	4.7	3.8	0.538
Myanmar	3437	5.4	7.6	3207	6.5	7.1	0.54
Angola	412	4.0	4.7	382	5.3	4.5	0.523
Swaziland	38	4.2	5.9	37	5.9	5.8	0.539
Tanzania (United Republic of)	2173	6.4	9.2	1986	8.4	8.6	0.513
Nigeria	286	0.3	0.3	262	0.4	0.3	0.514
Cameroon	123	0.9	1.0	118	1.3	1.0	0.501
Madagascar	908	5.1	7.8	840	6.5	7.4	0.508
Zimbabwe	735	4.7	9.6	671	5.9	8.6	0.488
Mauritania	12	0.7	0.6	12	0.9	0.6	0.501
Solomon Islands	1	0.2	0.2	1	0.3	0.2	0.509
Papua New Guinea	108	1.5	2.8	96	1.9	2.6	0.506
Comoros	36	7.8	9.6	34	9.7	9.3	0.49
Yemen	462	4.1	4.3	431	5.1	4.1	0.498
Lesotho	192	12.4	15.1	178	15.4	13.9	0.484
Togo	104	2.8	3.0	99	3.6	2.9	0.47
Haiti	130	1.6	1.8	119	2.0	1.7	0.483
Rwanda	345	4.2	6.7	314	5.1	6.3	0.485
Uganda	2377	8.1	17.1	2159	10.0	15.9	0.478
Benin	40	0.8	0.8	37	1.0	0.7	0.466
Sudan	1055	5.2	5.3	971	6.3	5.0	0.478
Djibouti	22	3.8	3.9	22	5.1	3.9	0.464
South Sudan	538	6.2	9.4	496	7.5	8.8	0.417
Senegal	46	0.7	0.7	43	0.9	0.7	0.474

Continued Table 1. Number, Crude, and Standardized Incidence and Mortality Rates of Esophageal Cancer in World in 2012

Countries	Incidence Rate			Mortality Rate			HDI
	Number	Crud rate	ASR (W)	Number	Crud rate	ASR (W)	
Afghanistan	1326	6.6	9.6	1217	7.9	9.0	0.47
Malawi	1969	12.8	24.2	1799	16.1	22.9	0.459
Ethiopia	1622	2.7	3.4	1506	3.3	3.2	0.427
Congo (Democratic Republic of the)	1130	3.0	3.7	840	6.5	7.4	0.412
Liberia	13	0.6	0.7	13	0.8	0.7	0.419
Guinea-Bissau	3	0.4	0.4	3	0.5	0.4	0.415
Mali	74	0.8	0.9	69	1.0	0.9	0.421
Mozambique	520	3.9	7.1	474	4.7	6.6	0.405
Sierra Leone	16	0.6	0.8	16	0.7	0.8	0.413
Guinea	24	0.5	0.4	23	0.5	0.4	0.415
Burkina Faso	114	1.5	1.5	104	1.7	1.4	0.391
Burundi	572	8.1	12.8	528	9.3	12.2	0.398
Chad	103	1.7	1.8	94	2.0	1.7	0.387
Eritrea	110	3.6	4.5	102	4.4	4.3	0.414
Central African Republic	61	2.2	2.3	56	2.6	2.1	0.37
Niger	57	1.0	0.7	52	1.1	0.7	0.341

the cases worldwide occur in less developed regions. Esophageal cancer incidence rates worldwide in men are more than double those in women (male: female ratio 2.4:1). In both genders there are more than 20-fold differences in incidence between the different regions of the world, with rates ranging from 0.8 per 100,000 in Western Africa to 17.0 per 100,000 in Eastern Asia in men, and 0.2 per 100,000 in Micronesia/Polynesia to 7.8 per 100,000 in Eastern Africa in women. Cancer of the esophagus has a very poor survival (overall ratio of mortality to incidence of 0.88), and the esophageal cancer mortality closely follows the geographical patterns for incidence, with the highest mortality rates occurring in Eastern Asia (14.1 per 100,000) and Southern Africa (12.8) in men and in Eastern (7.3) and Southern Africa (6.2) in women (Figure 1, Figure 2).

The highest incidence and mortality rates of esophageal cancer were observed in low human development as 5.39 and 5.17 cases per 100000 people, respectively. Also, the lowest incidence and mortality rates of esophageal cancer were indicated in very high human development as 3.14

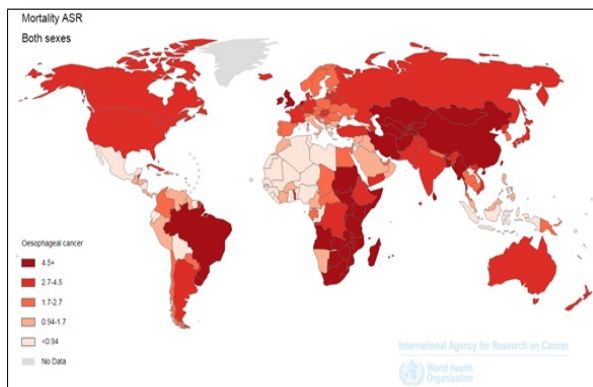


Figure 2. Distribution of the Standardized Mortality Rate of Esophageal Cancer in World at 2012 (Extracted from Globocan)

and 2.6 cases per 100000 people, respectively highest value of LEB, MYS, GNI, and total HDI were estimated to be 80.1, 11.7, 40045, and 0.86, respectively (Table 2).

A negative correlation was found between the incidence ( $R=-0.158$ ,  $P<0.05$ ) and mortality ( $R=-0.219$ ,  $P<0.05$ ) rates with HDI and esophageal cancer respectively. This amount was statistically significant (Figure 3).

The linear regression indicated that increased HDI, MYS, and GNI would decrease the incidence and mortality rates of esophageal cancer. This amount was not statistically significant ( $P>0.05$ ). The regression analysis showed that increased LBE would significantly decrease the incidence ( $B=-0.11$ ) and mortality rates ( $B=-0.12$ ) of esophageal cancer respectively (Table 3).

## Discussion

Cancer was considered as one of the most important mortality causes in the developing countries with the increasing incidence rate through changing the life style toward the western life style [18]. In 2017, May, the World Health Organization (WHO) emphasized a complex of actions in order to improve and accessibility increase to prophylaxis, early diagnosis, quick and available treatment as well as cancer ameliorating cares. The estimates indicated the increasing rate of cancer incidence as 45% till 2030 [19].

In 2001, more than 300000 cases of esophageal cancer were reported worldwide [15]. The regions' geographical diversity with the high incidence rates  $>3$  cases per 100000 people in western countries differs from the Central Asia with the incidence rate of 140 cases per 100000 people annually [20]. The highest rate of esophageal cancer was reported in China, Northern-East of Iran, Southern-East of the United States and South regions of Africa [21]. The reports indicated the increasing incidence rate of esophageal cancer in the 3 decades ago [22]. The incidence

Table 2. Esophageal Cancer Incidence and Mortality and HDI Component in Different HDI Regions in 2012

HDI	Incidence		Mortality		HDI Component			
	CR	ASR	CR	ASR	LEB	MYS	GNI	HDI
Very high human development	1.34	3.14	2.35	2.6	80.1	11.7	40045	0.86
High human development	2.01	3.25	2.93	2.8	74.35	8.2	13231	0.74
Medium human development	2.83	3.64	3.81	3.49	67.9	5.51	5960	0.63
Low human development	3.7	5.39	4.6	5.17	59.3	4.2	2904	0.46
P-value(F-test)	P<0.001	P<0.001	P<0.001	P<0.001	P<0.001	P<0.001	P<0.001	P<0.001

Abbreviations, CR, Crude Rate; ASR, Age-Standardized Rates per 100,000; HDI, Human Development Index; LEB, Life Expectancy at Birth; MYS, Mean Years of Schooling; GNI, Gross National Income per capita, PN.

Table 3. Effect of HDI Components and Demographic Variables on Esophageal Cancer Incidence and Mortality Rates

Demographic Variables	esophagus Cancer incidence			esophagus Cancer Mortality		
	B	CI95%	P-value	B	CI95%	P-value
HDI	-0.03	(-0.01, -0.09)	P>0.05	-0.03	(-0.01, -0.09)	P>0.05
Gross national income per 1000 capita	-0.004	(-0.001, 0.001)	P>0.05	-0.002	(-0.001, 0.009)	P>0.05
Mean years of schooling	-0.63	(-0.8, 1.8)	P>0.05	-0.53	(-0.9, 1.5)	P>0.05
Life expectancy at birth	-0.11	(-0.2, -0.02)	0.017	-0.12	(-0.2, -0.04)	0.002

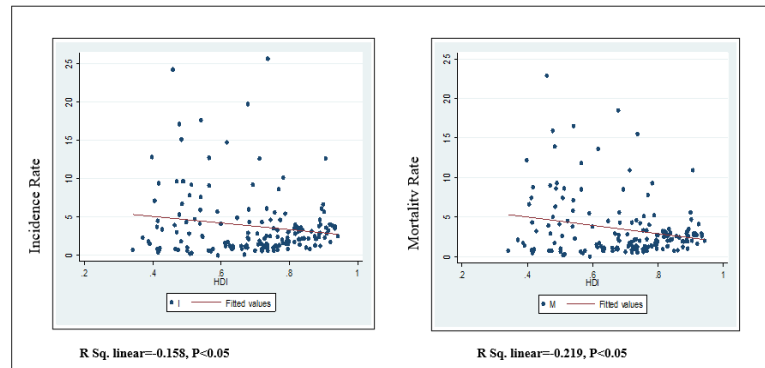


Figure 3. Correlation Between the Human Development Index and Esophageal Cancer Incidence and Mortality Rates in the World in 2012

rate of esophageal cancer was more observed in the developing countries than the developed countries [23]. The National Institute of cancer, US and International Agency of Cancer Research held an international workshop in 2016, September [23].

In 2012, some 450000 people were diagnosed with esophageal cancer (3.2% of the overall cancers) with a mortality rate of 400000 cases worldwide (4.9% of the overall cancers). This report shows the increasing incidence rate in the last decade. It is expected that the incidence rate would quickly be increased.

In 2012, the incidence rate of esophageal cancers was estimated as 45784 cases with the ratio of 3.2 cases per 100000 people worldwide. The incidence rates in males were higher than females being 323008 vs. 132776 cases with the ratios of 4.4 and 2 cases per 100000 people, respectively.

In 2008, some 47016 new cases of esophageal cancer with the mortality rate of 14280 cases were registered in the United States [24]. The time process in esophageal cancer is too different. For instance, while the incidence rate of esophageal squamous cell carcinoma in some Asian countries like Taiwan was increased [25] it was

continuously decreased in North America and Europe owing to the low consumption of Alcohol and smoking [26].

More than 80% of the esophageal cancer related-mortality was observed in the developing countries [23].

The incidence of esophageal cancer was observed higher in countries with lower HDI as compared to the lower incidence of esophageal cancer in countries with higher HDI owing to lifestyle and diet changes and lower smoking.

In 2012, the mortality rate of esophageal cancers was estimated as 400169 cases with the ratio of 5 cases per 100000 people worldwide.

Obesity, smoking, meat, alcohols and hubble-bubble, snuff, opioids, hot tea, low consumption of vegetables, fruits and poor socio-economic condition were considered as the risk factors of esophageal cancer [8, 27]. Tobacco usage, over-drinking, poor nutrition regimens of vegetables and fruits, low socio-economic condition in the United States and other western countries were related to esophageal cancer [19]. Alcohol and tobacco usage were not considered as the risk factors of esophageal cancer in Iran and China [28]. More studies in cancer causes might

help to determine the other potential factors providing the necessary information so as to enhance their growth.

Recently, the Nitrosamines were reported as the most stable factors of esophageal cancer. Nitrosamine and precursors compounds are available in preserves, vegetables, and salted fish [29].

The primary risk factors of squamous cell carcinoma in the western countries were considered as smoking and alcohol consumption applying some 90% of the overall cases. Smoking and alcohol consumption were reported as the esophageal cancer risk factors in the United States, Western Europe, and other regions of the world. Smoking and alcohol consumptions interfere with each other might increase the relative risk more than 100 folds.

The risk of esophageal cancer in smokers is 5 degree higher than non-smokers [10]. There is a direct correlation between number of cigarettes, smoking duration, and smoking with esophageal risk factor [30-31].

Obesity was reported as one of the most stable and consolidated risk factors of esophageal adenocarcinoma. The prevalence of esophageal adenocarcinoma was increased by increasing the rate of obesity in western countries. However, some of the studies report the paradox results. Increasing adipose following the obesity, affect the tumor's growth [32-33].

In a study performed in Sweden, an inverse correlation was reported between the regimen fibers consumption with digestive system adenocarcinoma. A study performed in the United States reported the nutrition contenting vitamins, fruits, and vegetables as a supportive factor against esophageal cancer incidence [29]. Malnutrition including low consumption of vitamins such as A, C, and E ones as well as riboflavin, zinc, selenium, and low consumption of fresh fruits and vegetables might play a role in increasing the disease's incidence [34].

In conclusion, the prophylactic actions to prevent the esophageal cancer are including keeping the healthy body weight, discontinue of smoking, low consumption of alcohol, and increasing the physical activity. In addition, a healthy regimen full of fresh fruits and vegetables might decrease the personal risk. More studies so as to diagnose the primary prophylactic actions in high risk regions (e.g., Northern regions of Iran, and Central Asia) are necessary to be performed.

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### Conflicts of interest

The authors declare no conflict of interest.

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