World Cancer Research Journal WCRJ 2019; 6: e1386

ESOPHAGUS CANCER GEOGRAPHICAL DISTRIBUTION, INCIDENCE, MORTALITY AND THEIR WORLD HUMAN DEVELOPMENT INDEX (HDI) RELATIONSHIP: AN ECOLOGY STUDY IN 2018

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Abstract – *Objective:* *Esophageal cancer is the eighth most common cancer in the world. About 80% of cases occur in less developed regions. The study purposed to investigate the epidemiology of esophageal cancer incidence and mortality in 185 countries and its relation with HDI in 2018.*

Materials and Methods: *A descriptive-analytical study was developed based on cancer incidence and mortality data extraction from the World Bank for Cancer in 2018. The incidence and mortality rates and esophagus cancer distribution maps were drawn for World countries. To analyze data, correlation and regression tests were used to evaluate the relationship between the incidence and mortality with HDI. The statistical analysis was carried out by Stata-14, and the significance level was estimated at 0.05 level.*

Results: The highest and the lowest esophageal cancer incidences were in the Asian continent (N=444597; 77.7%) and the Oceania continent (N=2315; 0.4%). The most esophageal cancer incidence and mortality was in high HDI regions. A negative and significant correlation was observed between incidence (R = -0.143, p <0.05) and mortality (R = 0.234, p <0.05) of esophagus cancer and HDI. Furthermore, there was a negative and significant correlation between incidence rate and LEB (r = -0.16, p <0.05). Also, the results showed a negative and significant correlation between mortality rate and GNI (r = 0.1, p <0.05), MYS (r = -0.17, p <0.05), LEB (r = -0.23, p <0.05) and EYS (r = -0.15, p <0.05).

Conclusions: *There is a negative correlation between esophageal cancer incidence and mortality as well as the HDI index, improving the HDI can be effective in reducing of the cancer incidence and mortality.*

KEYWORDS: *Geographical distribution, Incidence, Mortality, Esophageal cancer, HDI, World.*

INTRODUCTION

Esophageal cancer is the eighth most common cancer worldwide, with approximately 456000 new cases and 400000 deaths in 2012. Almost 80% of all esophageal cancers have occurred in less developed areas[1]. The main features of this cancer are low survival and rapid disease progression. The highest esophageal cancer rates in the world occurred in China, northeastern Iran, southeastern United States and South Africa. The Asian belt of cancer begins in eastern Turkey and northeastern Iran, and continues to reach eastern Asia countries, including the north and center of China. The cancer incidence

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in these areas is more than 100 per 100000 people[2]. Gender variability is significant in esophageal cancer incidence, so that, in men ranged from 0.8 in 100000 in West Africa to 17 in 100000 in East Asia while, in women it varies from 0.02 to 100000 in the center and south of Pacific Ocean to 7.8 in 100000 in eastern Africa[3,4]. Lifestyle is one of the most effective factors in esophageal cancer distribution. Esophageal cancer is heavily influenced by individuals' socioeconomic level. Individuals with low socioeconomic level are more likely to develop esophageal cancer due to inappropriate nutrition, excessive alcohol consumption, and more smoking. The importance of HDI in esophageal cancers incidence and mortality has been confirmed in numerous studies[5]. This work investigated the epidemiology of esophageal cancer incidence and morbidity as well as its relationship with the HDI in 185 countries in 2018.

MATERIALS AND METHODS

Due to quality limitation and existing cancer data coverage in the world, it is necessary to be cautious for interpretation of the data, especially in low and middle-income countries. The IARC approach is not just to evaluate, compile and use data from other institutions, but the center/organization intention is to work with country centers to improve the quality of native data, data coverage and analytical capacities. The urgent need for investment in the coverage of population-based cancer information in low and middle-income countries led to collaboration with the IARC for Global Cancer Registry Program (GICR) launching. The GICR aim is to provide information on cancer control, which can be regularly promoted through the coverage, quality, and use of population-based cancer data. A summary of the steps used to calculate the incidence, mortality and prevalence of the cancer is presented below. The calculation methods vary from countries and the national computing data quality depends on the coverage, accuracy, time of the outbreak, and deaths of each country.

INCIDENCE

The methods used to calculate the incidence associated with gender and age in each country, in order of priority, fall into the following broad categories: (1) - The reported national incidence rate was announced by 2018 (45 countries). (2) - The newest observation rates (national or regional) on the population were applied in 2018 (50 countries). (3) - The rates were calculated using national mortality data with modeling, as well as the mortality and morbidity ratio of the cancer record in that country (14 countries). (4) - The rates were calculated by national mortality using modeling, mortality rate and incidence of recorded cancer in neighboring countries (37 countries). (5) - The national incidence rate for age and gender for all cancers was obtained by averaging the overall rates of neighboring countries. Subsequently, these levels were partitioned to produce a national occurrence for each specific site using the relative cancer data frequency (7 countries). (6) - Rates were calculated as the average of selected neighboring countries.

MORTALITY

The methods used to calculate the cancer mortality rates associated with gender and age in each country are ranked in priority order in the following categories: (1) - National mortality rate monitored by the year 2018 was announced (81 countries). (2) - The latest national mortality rates observed on the population in 2018 (20 countries). (3) - Rates were calculated using data and through modeling assistance, as well as deaths' proportion on the recorded cancer prevalence in neighboring countries (81 countries). (4) - Rates were calculated as selected neighboring countries averages (3 countries)[6,7].

HDI

HDI is a three-dimensional indicator composite: life expectancy, study rates, and resources mastery needed to have a decent life. All groups and regions that could make a significant progress on all HDI components have grown faster than those with low or medium HDIs. As the indicator shows, the world is unequal, because national averages do not show different experiences of individuals' lives. There are countless inequalities in the northern and southern countries and inequalities in income have increased in each country as well as between different countries[5,8,9].

STATISTICAL ANALYSIS

In this study, the correlation bivariate method was used to assess the correlation between the incidence and mortality rates of esophageal cancer and the HDI. Linear regression models were also used to assess the HDI effect on the incidence rate of esophageal cancer. Significance level was considered lower than 0.05. Data analysis was conducted by Stata software version 14.

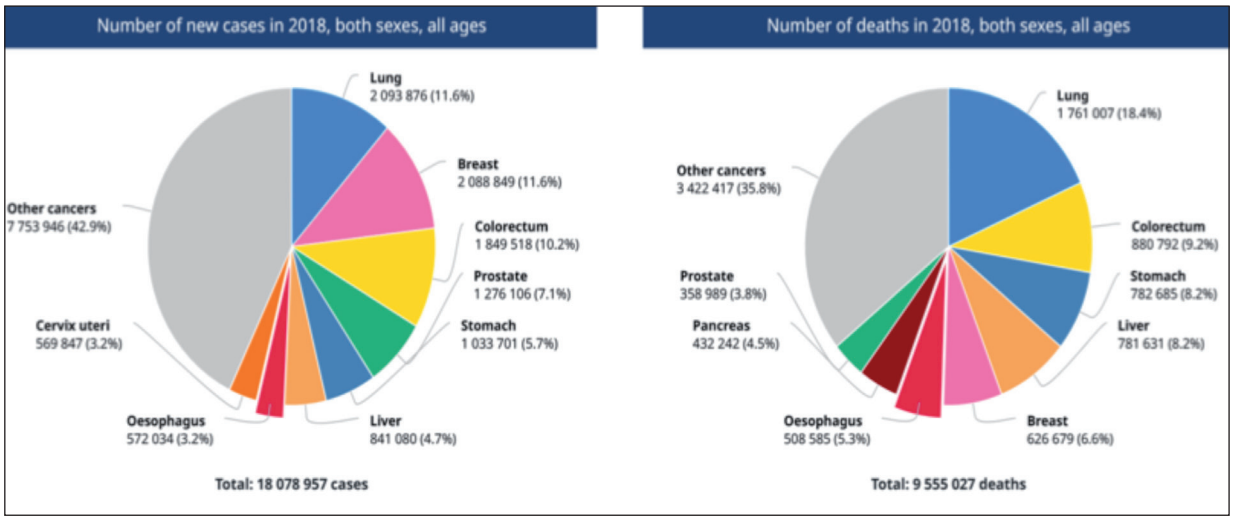

Fig. 1. Pie charts present the distribution incidence and mortality cancers in the world in 2018 for both sexes [Source: GLOBOCAN 2018].

RESULTS

According to the recorded cancer results in 2018, 18078957 new cases and 9555027 deaths were recorded due to cancer, of which 572034 new cases (3.2%) and 508585 (5.3%) died due to esophageal cancer (Figure 1).

The highest and the lowest esophageal cancer incidences were in the Asian continent (N=444597; 77.7%) and the Oceania continent (N=2315; 0.4%), respectively. Furthermore, the highest and the lowest mortality rates were observed for the Asia continent (N=397745; 78.2%) and the Oceania continent (N=1960; 0.39%) (Figure 2).

Recorded cancer incidence in 2018 showed that the highest esophageal cancers incidence, based on regional segmentation in both sexes, was related to high HDI (343605 cases); in men (239990 cases) and in women (103615 cases). Furthermore, the highest mortality rate of esophageal cancer in both genders was also recorded in high HDI regions (312604 cases); in men (219438 cases) and in women (93166 cases) (Table 1).

The results showed that the highest esophageal cancer incidence in the world was recorded in Malawi (18.7), Mongolia (18.5), and Kenya (18.4) per 100000, respectively. However, the highest mortality rate was observed in Kenya (18.4), Malawi (18.3), and Mongolia (16.3) in 100000, respectively (Table 1, Figure 3).

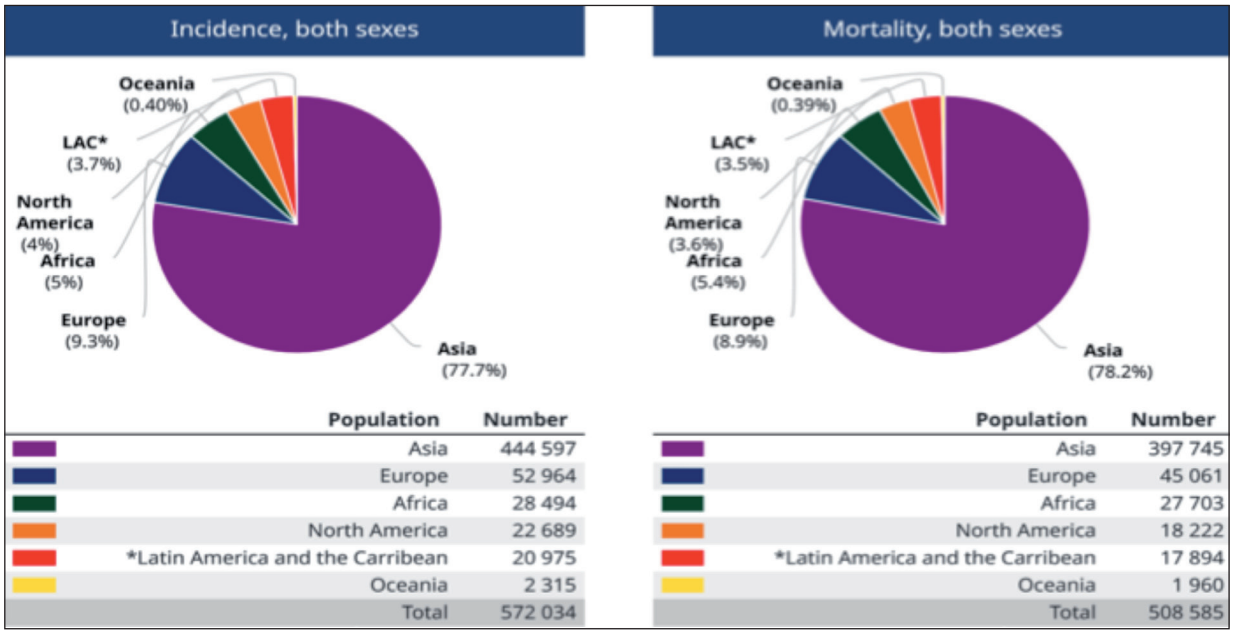

Fig. 2. Pie charts present the distribution of cases and deaths by continent in 2018 for both sexes [Source: GLOBOCAN 2018].

TABLE 1. Incidence and mortality esophagus cancer statistics worldwide and by region in 2018.

	Incidence						Mortality					
	Both sex		**Meal**		**Female**		**Both sex**		**Meal**		**Female**	
Countries	**New cases**	**Cum. Risk (%)**	**New cases**	**Cum. Risk (%)**	**New cases**	**Cum. Risk (%)**	**New cases**	**Cum. Risk (%)**	**New cases**	**Cum. Risk (%)**	**New cases**	**Cum. Risk (%)**
Eastern Africa	17792	0.97	9657	1.12	8135	0.84	17564	0.96	9574	1.11	7990	0.83
Middle Africa	1564	0.22	855	0.24	709	0.21	1450	0.22	772	0.24	678	0.2
Northern Africa	3093	0.18	1627	0.2	1466	0.17	2900	0.17	1509	0.18	1391	0.16
Southern Africa	3913	0.82	2331	1.19	1582	0.55	3793	0.8	2297	1.17	1496	0.52
Western Africa	2132	0.12	1358	0.17	774	0.08	1996	0.12	1292	0.17	704	0.07
Caribbean	1882	0.4	1488	0.67	394	0.15	1645	0.34	1315	0.59	330	0.12
Central America	1756	0.11	1289	0.18	467	0.05	1661	0.11	1257	0.18	404	0.04
South America	17337	0.39	12673	0.64	4664	0.17	14588	0.32	10935	0.55	3653	0.13
North America	22689	0.41	18052	0.69	4637	0.14	18222	0.3	14564	0.53	3658	0.1
Eastern Asia	335080	1.3	237160	2.22	97920	0.85	300878	1.32	212430	1.92	88448	0.72
South-Eastern Asia	12864	0.22	10418	0.38	2446	0.08	11857	0.21	9614	0.36	2243	0.07
South-Central Asia	92741	0.62	58395	0.8	34346	0.45	81432	0.55	53404	0.74	28028	0.37
Western Asia	3912	0.2	2055	0.23	1857	0.17	3578	0.18	1924	0.21	1654	0.15
Central and Eastern	15616	0.37	12723	0.74	2893	0.1	14140	0.33	11631	0.67	2509	0.08
Europe												
Western Europe	17980	0.53	13732	0.86	4248	0.22	14423	0.38	11177	0.64	3246	0.14
Southern Europe	6449	0.23	5153	0.41	1296	0.07	5644	0.19	4545	0.33	1099	0.05
Northern Europe	12919	0.66	9059	1.04	3860	0.31	10854	0.5	7579	0.79	3275	0.22
Australia/New Zealand	2048	0.41	1492	0.65	556	0.17	1708	0.31	1201	0.49	507	0.13
Melanesia	238	0.41	155	0.59	83	0.26	227	0.4	147	0.58	80	0.26
Polynesia	17	0.32	17	0.65	0	0.0	13	0.26	13	0.52	0	0.0
Micronesia	12	0.31	10	0.5	2	0.13	12	0.31	10	0.5	2	0.13
Low Human Development	19975	0.45	10748	0.51	9227	0.4	19406	0.44	10446	0.5	8960	0.39
Medium Human Development	104697	0.51	67863	0.68	36834	0.34	95585	0.46	63849	0.64	31736	0.29
High Human Development	343605	1.24	239990	1.81	103615	0.7	312604	1.09	219438	1.61	93166	0.6
Very High Human Development	103613	0.46	80988	0.79	22625	0.16	80865	0.33	63361	0.58	17504	0.1
World	572034	0.78	399699	1.15	172335	0.43	508585	0.67	357190	1.0	151395	0.36

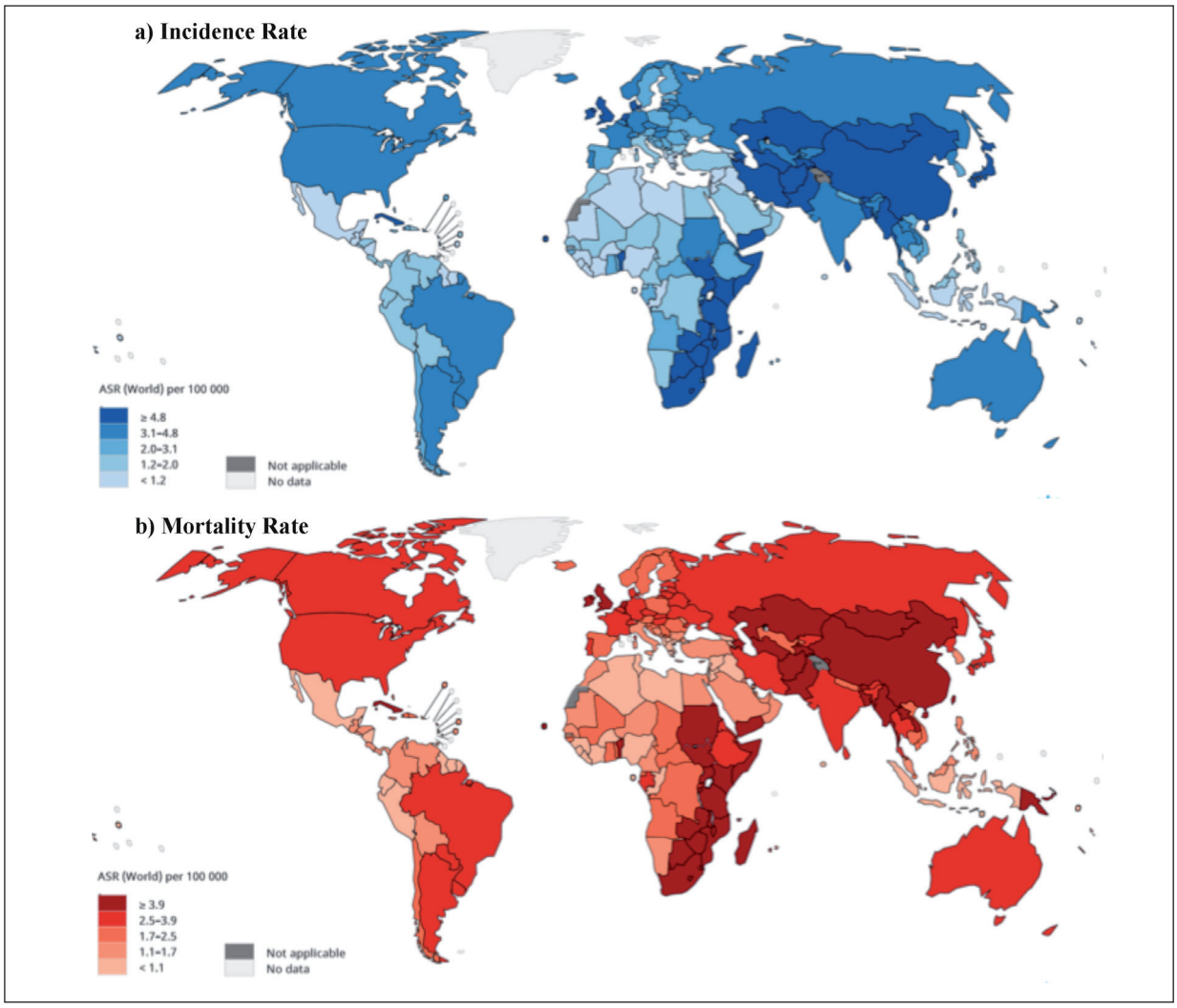

Fig. 3. Global map presenting (**a**) incidence and (**b**) mortality rates of esophagus cancer by world countries in 2018 [Source: GLOBOCAN 2018].

The variance analysis results showed that the highest mean of esophageal cancer incidence (1.4 per 100000) was related to Medium and low HDI and the lowest incidence mean (2.7 per 100000) was related to high HDI. In addition, the highest mortality mean (4.35 per 100000) was related to low HDI and the lowest mortality mean (2.3 per 100000) was for the high and very high HDI regions. The mean difference was statistically significant (p <0.001) for both incidence and mortality in different classes (Table 2).

TABLE 2. Esophagus cancer incidence and mortality in different HDI regions in 2018.

Human Development Index	Incidence Rate		Mortality Rate	
	CR	ASR	CR	ASR
Very high human development	5.7	2.9	4.7	2.3
High human development	3.4	2.7	2.9	2.3
Medium human development	3	4.1	2.8	3.9
Low human development	2.06	4.1	2	4.03
p-value (F-test)	p <0.05	p >0.05	p <0.05	p <0.05

Abbreviations: CR: Crude Rate; ASR: Age-Standardized Rates per 100,000.

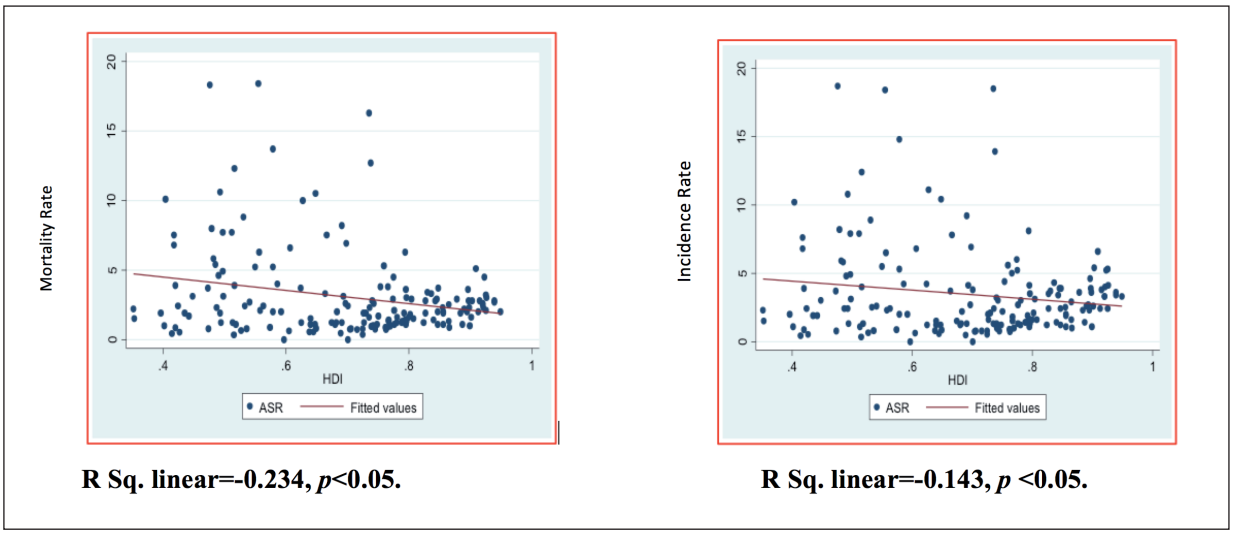

Fig. 4. Correlation between HDI, incidence and mortality rates of cancer esophagus in the world in 2018.

The results showed that there is a negative and significant correlation between incidence (R = -0.143, p <0.05), mortality (R = -0.234, p <0.05) of esophagus cancer and HDI index (Figure 4).

We documented that there is a negative and significant correlation between incidence rate and LEB (r = -0.16, p <0.05). Also, a negative and significant correlation was observed between mortality rate and GNI (r = 0.1, p <0.05), MYS (r = -0.17, p <0.05), LEB (r = -0.23, p <0.05) and EYS (r = -0.15, p <0.05) (Table 3).

DISCUSSION

We showed that esophageal cancer incidence is higher in lower HDI countries, and the most cases occur in less developed and developing countries, which can be due to lifestyle changes, smoking, alcohol consumption, and inappropriate nutrition[10]. The results also showed that the highest incidence (N=444597; 77.7%) and mortality (N=397545; 78.2%) of esophageal cancer was in Asia continent and the highest incidence and mortality of esophageal cancer, based on regional division in both genders (N=343605) were in high HDI countries. There is considerable heterogeneity in the incidence, geographical distribution, ethnic pattern of esophageal cancer, and this incidence predominantly exists in developing countries. The incidence varies from over 100 per 100,000 in Asian-belted countries and 10 to 100,000 in developed countries such as the United States, Finland, and France[11]. In developed countries such as the United States, the incidence of esophageal cancer peaked in the early 1990s and has fallen since then. The reason for this decrease can be increased awareness, preventive measures, early diagnosis and new and more effective access to treatment regimens[12]. Other studies have shown that there is a large geographical variation in the epidemiological nature of esophageal cancer; the highest incidence is in East Asia and in East and Southern Africa and the lowest in West Africa[13]. The highest rates of esophageal cancer in Asian countries were in Turkmenistan, Mongolia, Tajikistan, Bangladesh and China. All these countries are part of the Asian belt of cancer. The incidence of cancer in this region was more than 100 per 100000 people[14] . Household wealth and income are another important factors associated with lifestyle, especially nutrition. Previous epidemiological studies have shown that excessive consumption of tobacco and alcohol, and lower consumption of fruits and vegetables is common among people with low income[15]. Our results showed a negative and significant correlation between incidence

TABLE 3. Pearson correlation between HDI component and dependent variable.

HDI	ASIR*		ASMR*	
	r	p -value	r	p -value
Gross national income per 1000 capita	-0.09	p >0.05	-0.15	p <0.05
Mean years of schooling	-0.09	p >0.05	-0.17	p <0.05
Life expectancy at birth	-0.16	p <0.05	-0.23	p <0.05
Expected years of schooling	-0.08	p >0.05	-0.15	p <0.05

(R = -0.143, p <0.05), mortality (R = 0.234, p <0.05) of esophageal cancer and HDI index. The study by Hu et al [13] showed that the incidence and mortality rate varies considerably in different regions. For example, the incidence rate in less developed regions, such as Africa with a lower HDI level (as a composite of esophageal cancer) has a higher incidence. Furthermore, Africa, with a relatively low HDI, had a higher mortality rate for most gastrointestinal cancers, while North America, with higher HDI, showed lower mortality rates[16]. Individuals with a better socioeconomic status are less likely to develop morbidity and mortality due to more access to health services, such as clean water[17] . Increasing the use of tobacco products, such as hookahs and Nas, is associated with increased risk of SCC in the gastrointestinal tract. In addition, low socioeconomic status causes poor oral hygiene. There is a strong correlation between SCC and noncompliance with oral hygiene in Asian regions such as Kashmir and India[18, 19]. Other studies have shown that mortality due to cancer is higher in low and medium HDI countries[5]. The mortality in developed countries is decreased due to better treatment, screening using endoscopy, proper lifestyles, better access to health care and reduction of infectious diseases. In contrast, in developing and less developed countries, the cancer incidence and mortality are likely to be more due to poor lifestyles, smoking, alcohol, and lack of adequate infrastructure to implement comprehensive cancer control programs[3, 10] . The health literacy level is associated with reduced risk of developing cancer and behaviors such as drinking, smoking, physical inactivity, and poor lifestyle cause developing cancer[20] . Studies have shown that well educated individuals are more likely to seek out their health outcomes and early detection of cancer[20]. We showed a negative and significant correlation between incidence rate and LEB (r = -0.16, p <0.05). We also recorded a negative and significant correlation between mortality rate and GNI (r = 0.1, p <0.05), MYS (r = -0.17, p <0.05), LEB (r = -0.23, p <0.05 and EYS (r = -0.15, p <0.05). An important difference in esophageal cancer is gender differences; men are 3 to 4 times more likely to have cancer than women[21]. We documented that the esophageal cancer incidence and mortality in the world in men is almost twice that of women. This could be due to more tobacco and alcohol consumption among men than women. There are also many factors to explain the lower esophageal cancer incidence in women than men. Among these factors, the potential role of estrogen protection, lower abdominal obesity, less incidence of food and gastroesophageal reflux. There is also mechanical theory of low intra-abdominal pressure due to lack of narrow belts usage by women can cause less esophageal cancer[21,22].

CONCLUSIONS

Considering the negative correlation between esophageal cancer incidence and mortality with HDI, attention to HDI index can be effective in the cancer incidence and mortality reduction. Teaching people about the risk factors of esophageal cancer, especially in men, and increasing the level of awareness and knowledge in countries with lower HDI can play a significant role in reducing the incidence and mortality of the cancer.

Author Contributions:
The research design, E. V. and G. B. have designed this study. A. F. and F.C. have product the samples. Methodology, and analytical test were performed by M. R. C.; software, X.X.; validation, G:B and A.V., X.X.; supervision, by F.F.

Funding:
Not have

Acknowledgments:
Acknowledgements The authors gratefully acknowledge the many cancer registries worldwide and their staff for their willingness to contribute their data to this exercise.

Conflict of interest:
The authors declare no conflict of interest.

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