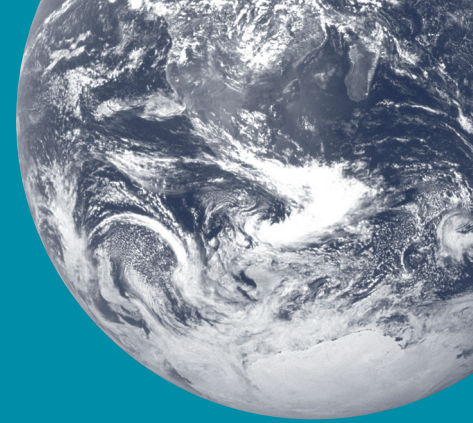




INCIDENCE AND MORTALITY OF GALLBLADDER CANCER AND ITS RELATIONSHIP WITH HUMAN DEVELOPMENT INDEX (HDI) IN ASIA IN 2012

N. MAHDAVIFAR¹, A. MOHAMMADIAN-HAFSHEJANI², M.GHAFARI³, H. SALEHINIYA^{4,5}

¹Department of Epidemiology and Biostatistics, Health Promotion Research Center, School of Public Health, Zahedan University of Medical Sciences, Zahedan, Iran

²Department of Public Health, School of Public Health, Dezful University of Medical Sciences, Dezful, Iran

³Department of Public Health, School of Public Health, Shahrekord University of Medical Sciences, Shahrekord, Iran

⁴Zabol University of Medical Sciences, Zabol, Iran

⁵Department of Epidemiology and Biostatistics, School of Public Health, Teheran University of Medical Sciences, Teheran, Iran

Abstract – Objective: Gallbladder cancer is a deadly malignancy, the sixth gastrointestinal cancer and one of the most common cancers of the biliary tract. This study aimed at investigating the incidence and mortality rate of gallbladder cancer and its relationship with Human Development Index (HDI) in Asia in 2012.

Methods: This study was an ecologic study in Asia for the assessment of the correlation between Standard Incidence Rate (SIR) and Standard Mortality Rate (SMR) with HDI and its components, which include: life expectancy at birth, mean years of schooling and Gross National Income (GNI) per capita. Statistical analyses were performed using SPSS (Version 15.0, SPSS Inc., Chicago, IL, USA).

Results: Overall, 116,048 cases of gallbladder cancer have been recorded in Asian countries in 2012. Countries with the highest SIR per 100,000 were Republic of Korea (6.5), Lao PDR (4.8), Japan (4.7), Nepal (4.3), Bangladesh (4.2) and the highest SMR were observed in Republic of Korea (4.8), Lao PDR (4.7), Nepal (4.1), Bangladesh (4), and Japan (3.9). There was a positive correlation between the SIR of Gallbladder cancer and HDI ($r = 0.032$, $p = 0.832$), whereas there was a negative correlation between the SMR of Gallbladder cancer and HDI ($r = -0.117$, $p = 0.438$).

Conclusions: Countries that have the highest SIR and SMR of gallbladder cancer do not have HDI levels associated with them since they span the ranks of countries with very high, medium, and low HDIs. A significant relationship was not observed between the SIR and SMR of gallbladder cancer and the HDI.

KEYWORDS: Gallbladder cancer, HDI, Asia, Incidence, Mortality.

INTRODUCTION

Cancers are one of the non-communicable diseases that present the community with a major disease burden¹. More than 70% of deaths that occur in both developing and developed countries have been linked to cancer². One of these cancers is gallbladder cancer, which is a fatal malignancy³. Gallbladder cancer is not

only the sixth most prevalent gastrointestinal cancer but also one of the most common cancers of the biliary tract. Its annual rate is 2.2 per 100,000 people around the world among rare and high-risk gastrointestinal cancers^{1,4}. In addition, the incidence of gallbladder cancer is high in many parts of the world including Chile, Peru, Bolivia, Korea, Japan, the Czech Republic, Slovakia, Spain, and India⁵. Despite



this, the incidence of this cancer is variable in different geographical areas. For example, in Chile this disease is the leading cause of cancer deaths in women⁶. In general, gallbladder cancer is more common in women while bile duct cancer is seen more frequently in men⁷.

Based on previous studies, we can consider a number of potential risk factors that have been associated with gallbladder cancer including a history of gallstones or gallbladder disease⁸, diet, tobacco use, exposure to wood or coal dust, long interval between meals, obesity, use of oral contraceptives, number of births, a family history of gallbladder disease⁹, and genetic factors¹⁰. According to published studies, gallstones are present in 70% to 94% of patients with gallbladder cancer^{5,11}. Due to both the anatomical location of the gallbladder and nonspecific symptoms of gallbladder cancer, the diagnosis of gallbladder cancer is usually made in the late stage of the disease accompanied by a poor prognosis. The negative impact of delayed diagnosis is supported by the findings of several studies that report the five-year survival rate to range from 5% to 12%¹²⁻¹⁵.

One of the criteria used to evaluate both diseases and deaths between countries is the HDI. In fact, this indicator is associated with both the incidence and mortality of many diseases and is an appropriate source of information to learn a country's status regarding a specific disease¹⁶. Although communicable diseases and nutrition are common causes of death in countries with a low HDI, it is forecasted that before 2030, deaths from non-communicable diseases such as cancer, will overtake those from communicable diseases, thereby attaining more crucial positions¹⁷. The relationship between the HDI and some types of cancer has been studied¹⁸⁻²⁶; investigating this relationship can lead to a more accurate understanding of the distribution of cancer and its risk factors²⁷. Knowledge about the incidence and mortality of gallbladder cancer can be useful for the design and implementation of health programs and research activities because of the probable role of the HDI. The aim of this study was to investigate the incidence and mortality rate of gallbladder cancer and its relationship with the Human Development Index (HDI) and components in Asia in 2012.

METHODS

This study was an ecologic study in Asia to assess the correlation between the standard incidence rate (SIR) and the standard mortality rate (SMR)

with Human Development Index (HDI) and its components, including life expectancy at birth, mean years of schooling, and the Gross National Income (GNI) per capita. Data about the SIR and the SMR for every country in 2012 were obtained from the Global Cancer Project available at (<http://globocan.iarc.fr/Default.aspx>)²⁸ and the HDI from the Human Development Report 2013²⁹ that includes information about the HDI and its components for every country in the world in 2012. The Human Development Index (HDI) is a composite measure of key indicators along three dimensions, including life expectancy, educational attainment, and command over resources needed for a decent standard of living²⁹.

Methods for estimating the incidence and mortality rates in the Global Cancer Project by the International Agency for Research on Cancer were published previously^{1,28}.

Statistical Analysis

In this study, we used a bivariate correlation method to assess the correlation between the SIR and the SMR with the HDI. Statistical significance was assumed if $p < 0.05$. All reported p -values are two-sided. Statistical analyses were performed using SPSS (version 15.0, SPSS Inc., Chicago, IL, USA).

RESULTS

Overall, 116,048 cases of gallbladder cancer were recorded in Asian countries in 2012. Of these cases, about 52,668 (45.38%) cases were in men, and 63,380 cases (54.61%) were in women. The sex ratio of developing the disease is 0.83 (men to women). The five countries with the highest number of new cases of gallbladder cancer are 1- China with 51,463 cases, 2- Japan with 21,417 cases, 3- India with 18,787 cases, 4- the Republic of Korea with 5,228 cases, and 5- Bangladesh with 4,712 cases. Therefore, these five countries represent 101,607 cases or 87.55% of all gallbladder cancer cases in Asia.

The five countries that have the highest SIR of gallbladder cancer per hundred thousand people in Asian countries are 1- the Republic of Korea with 6.5, 2- Lao PDR with 4.8, 3- Japan with 4.7, 4- Nepal with 4.3, and 5- Bangladesh with 4.2. In contrast, five countries that have the lowest SIR of gallbladder cancer per hundred thousand people are Maldives with zero and Yemen, Tajikistan, Turkmenistan, and Uzbekistan with 0.1 (Table 1).

TABLE 1. Number and rate of crude and SIR of gallbladder cancer in Asian countries in 2012 (based on GLOBOCAN 2012).

Population	Gallbladder - Estimated incidence all ages								
	Both sexes			Male			Female		
	Numbers	Crude rate	ASR (W)	Numbers	Crude rate	ASR (W)	Numbers	Crude rate	ASR (W)
Afghanistan	120	0.4	0.8	35	0.2	0.5	85	0.5	1.2
Armenia	29	0.9	0.6	13	0.9	0.7	16	1.0	0.5
Azerbaijan	46	0.5	0.5	23	0.5	0.5	23	0.5	0.4
Bahrain	6	0.4	0.8	3	0.4	0.8	3	0.6	0.9
Bangladesh	4712	3.1	4.2	1217	1.6	2.2	3495	4.6	6.2
Bhutan	11	1.5	2.1	5	1.3	1.9	6	1.7	2.3
Brunei	3	0.7	1.1	2	1.0	1.1	1	0.5	1.1
Cambodia	229	1.6	2.3	104	1.5	2.6	125	1.7	2.2
China	51463	3.8	2.8	23764	3.4	2.7	27699	4.2	2.9
Georgia	35	0.8	0.5	19	0.9	0.6	16	0.7	0.4
India	18787	1.5	1.8	7615	1.2	1.5	11172	1.8	2.1
Indonesia	1644	0.7	0.8	823	0.7	0.9	821	0.7	0.7
Iran, Islamic Republic of	753	1.0	1.2	328	0.9	1.0	425	1.1	1.4
Iraq	156	0.5	0.9	65	0.4	0.9	91	0.5	0.9
Israel	177	2.3	1.5	92	2.4	1.8	85	2.2	1.2
Japan	21417	16.9	4.7	10818	17.6	5.8	10599	16.3	3.7
Jordan	93	1.4	2.4	36	1.1	1.8	57	1.8	3.1
Kazakhstan	41	0.3	0.2	19	0.2	0.3	22	0.3	0.2
Korea, Democratic Republic of	764	3.1	2.4	325	2.7	2.7	439	3.5	2.3
Korea, Republic of	5228	10.8	6.5	2718	11.2	7.8	2510	10.3	5.4
Kuwait	17	0.6	1.1	9	0.5	1.1	8	0.7	1.3
Kyrgyzstan	40	0.7	1.1	13	0.5	0.9	27	1.0	1.2
Lao PDR	193	3.0	4.8	120	3.8	6.5	73	2.3	3.4
Lebanon	74	1.7	1.6	28	1.3	1.3	46	2.1	1.8
Malaysia	248	0.8	1.0	112	0.8	0.9	136	0.9	1.1
Maldives	0	0.0	0.0	0	0.0	0.0	0	0.0	0.0
Mongolia	9	0.3	0.5	5	0.4	0.5	4	0.3	0.4
Myanmar	1210	2.5	2.7	358	1.5	1.7	852	3.4	3.6
Nepal	904	2.9	4.3	331	2.2	3.6	573	3.7	4.9
Oman	12	0.4	0.7	7	0.4	0.6	5	0.4	0.8
Pakistan	1839	1.0	1.5	543	0.6	0.9	1296	1.5	2.2
Philippines	342	0.4	0.5	154	0.3	0.5	188	0.4	0.5
Qatar	11	0.6	2.1	7	0.5	1.9	4	0.9	2.7
Saudi Arabia	309	1.1	1.9	104	0.7	1.2	205	1.6	2.8
Singapore	138	2.6	1.7	67	2.5	1.8	71	2.7	1.7
Sri Lanka	163	0.8	0.6	86	0.8	0.7	77	0.7	0.5
State of Palestine	59	1.4	2.8	16	0.7	1.6	43	2.0	4.0
Syrian Arab Republic	237	1.1	1.7	92	0.9	1.4	145	1.4	2.0
Tajikistan	5	0.1	0.1	2	0.1	0.1	3	0.1	0.1
Thailand	2794	4.0	3.0	1590	4.6	3.7	1204	3.4	2.3
Timor-Leste	14	1.2	2.5	10	1.7	3.8	4	0.7	1.3
Turkey	1260	1.7	1.8	747	2.0	2.3	513	1.4	1.3
Turkmenistan	4	0.1	0.1	2	0.1	0.1	2	0.1	0.1
United Arab Emirates	28	0.3	1.4	19	0.3	1.5	9	0.4	1.2
Uzbekistan	28	0.1	0.1	11	0.1	0.1	17	0.1	0.1
Viet Nam	386	0.4	0.5	211	0.5	0.5	175	0.4	0.4
Yemen	10	0.0	0.1	0	0.0	0.0	10	0.1	0.2

On the other hand, 98,643 deaths have occurred due to gallbladder cancer in Asia during 2012. Of these deaths, 44,198 cases (44.80%) were in men, and 54,445 cases (55.19%) were in women. The sex ratio of gallbladder cancer mortality is 0.81. Of these, most deaths have oc-

curred in China with 41,973 cases, Japan with 19,309 cases, India with 15,866 cases, Bangladesh with 4,412 cases, and the Republic of Korea with 4,176 cases. Therefore, a total of 85,736 cases (86.91%) of deaths have occurred in just these five countries.



The five countries that have the highest SMR of gallbladder cancer per hundred thousand people in Asian countries are 1- the Republic of Korea with 4.8, 2- Lao PDR with 4.7, 3- Nepal with 4.1, 4- Bangladesh with 4, and 5- Japan with 3.9.

In contrast, the five countries that have the lowest SMR of gallbladder cancer per hundred thousand people are Brunei and Maldives with the amount of zero, and Yemen, Tajikistan, and Turkmenistan with 0.1 (Table 2).

TABLE 2. Number and rate of crude and SMR of gallbladder cancer in Asian countries in 2012 (based on GLOBOCAN 2012).

Population	Gallbladder - Estimated mortality all ages								
	Both sexes			Male			Female		
	Numbers	Crude rate	ASR (W)	Numbers	Crude rate	ASR (W)	Numbers	Crude rate	ASR (W)
Afghanistan	113	0.3	0.8	32	0.2	0.5	81	0.5	1.1
Armenia	28	0.9	0.6	13	0.9	0.7	15	0.9	0.5
Azerbaijan	42	0.4	0.4	21	0.4	0.5	21	0.4	0.4
Bahrain	1	0.1	0.2	0	0.0	0.0	1	0.2	0.5
Bangladesh	4412	2.9	4.0	1153	1.5	2.1	3259	4.3	5.9
Bhutan	11	1.5	2.1	5	1.3	1.9	6	1.7	2.3
Brunei	0	0.0	0.0	0	0.0	0.0	0	0.0	0.0
Cambodia	215	1.5	2.2	99	1.4	2.6	116	1.6	2.0
China	41973	3.1	2.3	19498	2.8	2.2	22475	3.4	2.3
Georgia	33	0.8	0.4	18	0.9	0.6	15	0.7	0.3
India	15866	1.3	1.5	6416	1.0	1.3	9450	1.6	1.8
Indonesia	1538	0.6	0.7	769	0.6	0.8	769	0.6	0.7
Iran, Islamic Republic of	707	0.9	1.1	306	0.8	0.9	401	1.1	1.3
Iraq	145	0.4	0.9	61	0.4	0.9	84	0.5	0.9
Israel	73	0.9	0.6	24	0.6	0.5	49	1.3	0.7
Japan	19309	15.3	3.9	9282	15.1	4.7	10027	15.5	3.3
Jordan	86	1.3	2.2	33	1.0	1.7	53	1.7	2.8
Kazakhstan	40	0.2	0.2	18	0.2	0.3	22	0.3	0.2
Korea, Democratic Republic of	641	2.6	2.0	283	2.3	2.4	358	2.9	1.8
Korea, Republic of	4176	8.6	4.8	2059	8.5	5.8	2117	8.7	4.0
Kuwait	11	0.4	0.8	5	0.3	0.4	6	0.5	1.4
Kyrgyzstan	38	0.7	1.0	12	0.4	0.8	26	0.9	1.1
Lao PDR	185	2.9	4.7	114	3.6	6.3	71	2.2	3.3
Lebanon	70	1.6	1.5	27	1.3	1.3	43	2.0	1.6
Malaysia	150	0.5	0.6	72	0.5	0.6	78	0.5	0.6
Maldives	0	0.0	0.0	0	0.0	0.0	0	0.0	0.0
Mongolia	7	0.2	0.3	4	0.3	0.4	3	0.2	0.3
Myanmar	1140	2.3	2.6	338	1.4	1.7	802	3.2	3.4
Nepal	847	2.7	4.1	311	2.0	3.4	536	3.4	4.7
Oman	12	0.4	0.7	7	0.4	0.6	5	0.4	0.8
Pakistan	1721	1.0	1.4	506	0.6	0.9	1215	1.4	2.1
Philippines	256	0.3	0.4	117	0.2	0.4	139	0.3	0.4
Qatar	10	0.5	2.0	6	0.4	1.8	4	0.9	2.7
Saudi Arabia	288	1.0	1.8	96	0.6	1.1	192	1.5	2.7
Singapore	75	1.4	0.9	28	1.1	0.7	47	1.8	1.1
Sri Lanka	153	0.7	0.6	80	0.8	0.6	73	0.7	0.5
State of Palestine	55	1.3	2.7	16	0.7	1.7	39	1.9	3.8
Syrian Arab Republic	219	1.0	1.6	85	0.8	1.3	134	1.3	1.9
Tajikistan	5	0.1	0.1	2	0.1	0.1	3	0.1	0.1
Thailand	2381	3.4	2.5	1356	3.9	3.2	1025	2.9	2.0
Timor-Leste	13	1.1	2.3	9	1.5	3.4	4	0.7	1.3
Turkey	1175	1.6	1.7	693	1.9	2.2	482	1.3	1.3
Turkmenistan	4	0.1	0.1	2	0.1	0.1	2	0.1	0.1
United Arab Emirates	25	0.3	1.3	17	0.3	1.4	8	0.3	1.1
Uzbekistan	27	0.1	0.1	11	0.1	0.1	16	0.1	0.1
Viet Nam	358	0.4	0.4	194	0.4	0.5	164	0.4	0.4
Yemen	9	0.0	0.1	0	0.0	0.0	9	0.1	0.1

Relationship between the SIR and the HDI

A positive correlation of 0.032 was observed between the SIR of gallbladder cancer and the HDI, but this association was not statistically significant ($p = 0.832$). In contrast, a correlation was observed between dimensions of the HDI and the SIR, so that a positive correlation of 0.2 existed between the SIR and life expectancy at birth ($p = 0.183$), a negative correlation of 0.152 was present with mean years of education ($p = 0.312$), and income level per person of the population had a positive correlation of 0.103 ($p = 0.495$) (Figure 1).

Relationship between the SIR and the HDI in men

In addition, a positive correlation of 0.144 was seen between the SIR of gallbladder cancer and the HDI in men, but this association was not statistically significant ($p = 0.341$). A positive correlation was also observed between the dimensions of the HDI and the SIR. Similarly, a positive correlation of 0.241 was seen between the SIR and both life expectancy at birth ($p = 0.107$) and income level per person of the population 0.144 ($p = 0.339$). In contrast, a negative correlation of 0.040 was seen with mean years of education ($p = 0.790$).

Relationship between the SIR and the HDI in women

A negative correlation of 0.085 was seen between the SIR of gallbladder cancer and the HDI in women, but this association was not statistically significant ($p = 0.573$). Also, a correlation was observed

between the dimensions of the HDI and the SIR, so that a positive correlation of 0.122 was seen between the SIR and life expectancy at birth ($p = 0.420$), a negative correlation of 0.252 was observed with mean years of education ($p = 0.091$), and a positive correlation of 0.074 was seen with income level per person of the population ($p = 0.626$).

Relationship between the SMR and the HDI

A negative correlation (0.117) was observed between the SMR of gallbladder cancer and the HDI, but this association was not statistically significant ($p = 0.438$). In addition, a correlation was observed between the dimensions of the HDI and standardized mortality rates. In fact, the correlation was positive between the SMR and both life expectancy at birth 0.078 ($p = 0.606$), and income level per person of the population. This positive correlation was 0.003 ($p = 0.983$), while there was a negative correlation with mean years of education 0.271 ($p = 0.568$) (Figure 2).

Relationship between the SMR and the HDI in men

A negative correlation of 0.018 was seen between the SMR of gallbladder cancer and the HDI in men, but this association was not statistically significant ($p = 0.908$). Also, a correlation was observed between the dimensions of the HDI and the SMR. A positive correlation of 0.110 was seen between the SMR and life expectancy at birth ($p = 0.469$), a negative correlation of 0.162 was observed with mean years of education ($p = 0.283$), and a positive correlation of 0.021 was seen with income level per person of the population ($p = 0.891$).

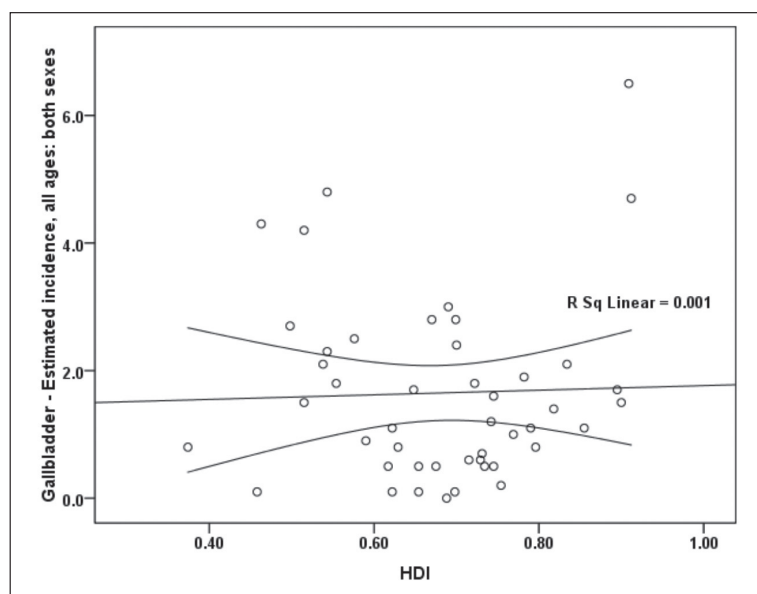


Fig. 1. The correlation between the SIR and HDI of gallbladder cancer in Asia in 2012.

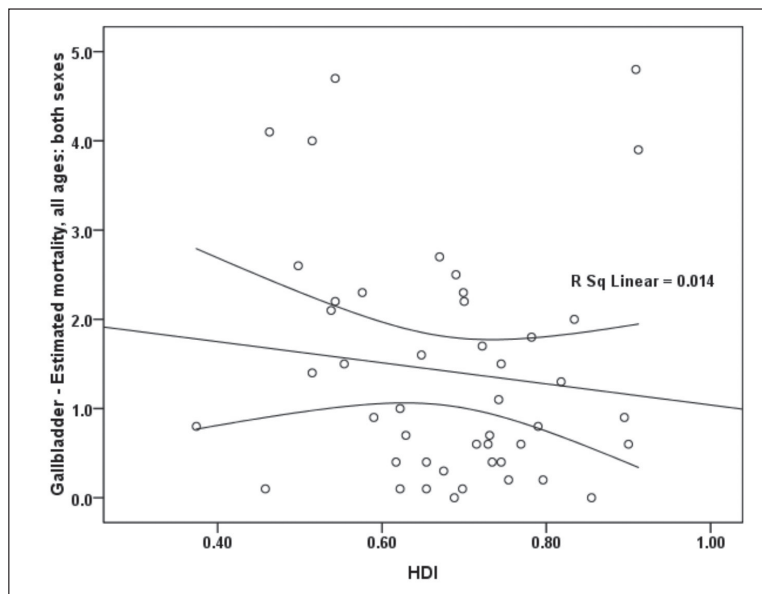
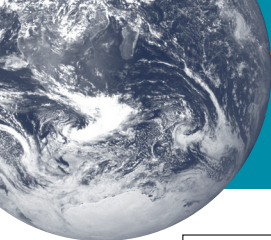


Fig. 2. The correlation between the SMR and HDI of gallbladder cancer in Asia in 2012.

Relationship between the SMR and the HDI in women

A negative correlation of 0.180 was seen between the SIR of gallbladder cancer and the HDI in women, but this association was not statistically significant ($p = 0.232$). In addition, a correlation was observed between the components of the HDI with the SMR, so that a positive correlation of 0.045 was seen between the SMR and life expectancy at birth ($p = 0.765$), a negative correlation of 0.334 was seen with mean years of education ($p = 0.023$), and a positive correlation of 0.022 was observed with income level per person of the population ($p = 0.885$).

DISCUSSION

Overall, 116,048 new cases and 98,643 deaths from gallbladder cancer were recorded in Asia in 2012. The sex ratio of developing the disease (male to female) was 0.83 and the sex ratio of deaths from gallbladder cancer was 0.81. Both the incidence and mortality of this cancer are different in diverse geographical areas and disparate ethnic groups^{5,33}, because of differences in risk factors related to disease progression and clinical symptoms at diagnosis in different areas^{5,34}.

In this study, countries that have the highest standardized rates of gallbladder cancer are in the ranks of countries with a very high HDI (Japan and the Republic of Korea), countries with an average HDI (Bangladesh and Lao PDR), and a low HDI (Nepal). In Japan, with a relatively high

prevalence, gallbladder cancer is responsible for 3.5% of deaths in women and 1.25% in men³⁵. Also, according to a recent report by the Council of Medical Research, India is one of the countries with the highest incidence of this cancer in the world. The incidence in Northern India is more than nine per 100,000 women per year³⁶. The basis for the difference in incidence is because of differences in the distribution of risk factors such as geographical location, genetic predisposition^{11,37}, dietary habits, fertility, age, and gender (four to seven times more common in women than in men)³⁸.

In this study, countries that have the highest SMR of gallbladder cancer also include countries with a very high HDI (Japan and the Republic of Korea), with a high HDI (China), and with an average HDI (Bangladesh and India). India is known as one of the regions with the highest mortality rates in Asia³³. The mortality of gallbladder cancer is related to the stage of the disease when the diagnosis is made. For example, if the disease is diagnosed from stage 0 to stage IV, then the five-year survival rate of this cancer can vary from 60% for stage 0 to 1% for stage IV of this cancer³. The highest mortality is associated with patients whose disease is diagnosed in stage III and higher³⁹. From an epidemiologic perspective, the incidence rate of gallbladder cancer is close to the mortality rate so that countries with the highest incidence, experience the highest mortality rates. Lack of access to health care and early diagnosis in some areas both contribute to these increases³⁴. In this study, no significant relationship was observed between the incidence and the mor-

tality of gallbladder cancer and the HDI. Also, a significant relationship was not seen between the standardized incidence rate and the standardized mortality rate of gallbladder cancer and dimensions of the HDI. However, according to previous studies, gallbladder cancer has been reported as a disease whose peak incidence in older women is during the 7th and 8th decades of life. Also, a study in India showed that this disease mainly occurs in women in the fourth decade of life, and after that because of the lower life expectancy of men⁴⁰. The reason why gallbladder cancer occurs at younger ages in Indian women may indicate a genetic predisposition in this population⁴¹.

In this study, no significant relationship has been observed between the SIR and the SMR of gallbladder cancer and HDI and its components (life expectancy at birth, mean years of schooling, and gross national income (GNI) per capita). Another study in Poland has introduced a low level of education as one of the main risk factors for these cancers⁴². In general, people with a low education are more affected by risk factors for this cancer⁴³. In countries with citizens who have a higher level of education, people typically have healthier habits and more wholesome behaviors that enable them to avoid cancer risk factors such as smoking and eating unhealthy diets, when compared with countries whose citizens have a lower level of education^{44,45}.

Another result of this study is that a significant relationship was not observed between the standardized incidence and mortality rate and appropriate income levels (GDP). According to previous studies, the precise roles of socioeconomic status and gallstones have been discussed⁶. Studies have shown that gallstones and low socioeconomic status are independent risk factors for both early onset and mortality of gallbladder cancer⁴⁶. Low socioeconomic status indirectly affects poor education, illiteracy, and may lead to joblessness. This resultant inability to pay for the costs of life and preventive healthcare services may adversely affect both the incidence and mortality of gallbladder cancer⁴⁷.

CONCLUSIONS

Countries that have the highest SIR and SMR of gallbladder cancer are in the ranks of countries with very high, medium and low HDI. A significant relationship was not observed between the SIR and SMR of gallbladder cancer, and the HDI.

CONFLICT OF INTERESTS:

The authors declared no competing interests.

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