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GLOBAL INCIDENCE AND MORTALITY OF LIVER CANCERS AND ITS RELATIONSHIP WITH THE HUMAN DEVELOPMENT INDEX (HDI): AN ECOLOGY STUDY IN 2018

E. GOODARZI[1], F. GHORAT[2], A. MOSAVI JARRAHI[3,4], H. A. ADINEH[5], M. SOHRABIVAFA[6], Z. KHAZAEI[7]

[1]Social Determinants of Health Research Center, Lorestan University of Medical Sciences, Khorramabad, Iran
[2]Iranian Research Center on Healthy Aging, Sabzevar University of Medical Sciences, Sabzevar, Iran
[3]Editor-in-Chief, Asia Pacific Journal of Cancer Prevention
[4]Faculty of Health Sciences, Simon Fraser University, Burnaby, BC, Canada
[5]Department of Epidemiology and Biostatistics, Iranshahr University of Medical Sciences, Iranshahr, Iran
[6]Dezful University of Medical Sciences, Dezful, Iran
[7]Department of Epidemiology, School of Public Health, Ilam University of Medical Sciences, Ilam, Iran

Abstract – *Introduction:* *Liver cancer is one of the most important and intensifying challenges of global health, especially in developing countries. The aim of this study was to evaluate the epidemiology of liver cancer incidence and mortality in 185 countries and determinate its relationship with the Human Development Index (HDI) in 2018.*

Materials and Methods: *The present study is a descriptive cross-sectional study that is based on extraction of cancer incidence data and cancer mortality rates from the World Bank for Cancer in 2018. The incidence and mortality rates and liver cancer distribution maps were drawn for World countries. To analyze data, correlation test 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: *According to the results of the cancer record in 2018, 18078957 cases of cancer were recorded, and 841080 cases (4.7% of all cancers) were related to liver cancer. The highest incidence and mortality of liver cancer was in Asia and in the countries of Mongolia and Egypt. The results showed that there is a negative correlation between incidence rate and mortality of liver cancer with HDI index. This correlation was not significant between the incidence rate of liver cancer and HDI index (r=-0.09, p>0.05). While there was a negative and significant correlation between liver cancer mortality and HDI index (r=-0.149, p<0.05). But this correlation was not significant in the development of disease (p>0.05). The results showed that there was a negative correlation between the incidence rate of liver cancer with GNI, MYS, LEB and EYS, which was not statistically significant (p> 0.05), while the correlation between mortality rate and MYS was significant (r=-0.154, p<0.05).*

Conclusions: *The highest incidence and mortality of liver cancer is related to the Asian continent. Therefore, attention to the development index, especially in the continents of Asia, can be effective in reducing the incidence and mortality of the disease.*

KEYWORDS: *Incidence, Mortality, Liver Cancer, HDI, World.*

INTRODUCTION

The primary cancer of the liver is the fifth most common cancer and the third cause of death from cancer in the world. In most countries, primary carcinoma of the liver cells accounts for about 75-90% of liver cancers[1,2]. It affects both sexes, but its prevalence in men (16 per 100,000) is more than in women (6 per

Corresponding Author: Zaher Khazaei, M.Sc.; e-mail: Zaherkhazaei@yahoo.com

100,000). The incidence of liver cancer is increased with age and the highest incidence is related to the age group of 60-70 years[3]. Liver cancer has a widespread distribution across the world and account for a serious threat to the people health. But the actual prevalence of the disease is still unknown in different parts of the world. The rate of liver cancer has been reported from 10 cases per 100,000 people in North America and Western Europe to 150 cases per 100,000 people in Africa and 50-70 cases in Asia[4-7]. Therefore, the highest incidence of liver cancer is in the regions of East Asia, Southeast and Central and Western Africa, and the lowest incidence is related to advanced countries (except South Europe)[2]. According to the annual statistics, more than 500,000 people every year catch this cancer and its 5-year mortality rate associated with this cancer is more than 95% per year, which is the highest mortality rate due to cancer. The most important causes of liver cancer in more than 75% of cases are chronic hepatitis C and B infections, which can be prevented [8-10]. In most cases, primary liver tumors occur in people with chronic liver disease (cirrhosis)[11]. In fact, chronic liver disease, inflammation, or cirrhosis of the liver in 70-90% of cases plays a role in the cancer of the liver cells. Exposure to aflatoxin, alcohol, tobacco, obesity, diabetes, birth control pills, insulin resistance, iron overload, hypothyroidism, lipid blood, and lipid peroxidation are other risk factors. Metastases of other cancers should also be considered [8,11,12]. Cancer is the third cause of death after cardiovascular diseases and accidents [13-15]. The incidence and mortality rate associated with liver cancer also has an increasing trend associated with the Human Development Index (HDI). This indicator consists of three dimensions of health, education and income, and indicates the level of economic and social well-being of the target population. Increased levels of obesity, type II diabetes, the prevalence of HCV and HBV infection, high prevalence of smoking, alcohol consumption and injections in relatively developed countries, and differences in life expectancy, low literacy rates, exposure to environmental pollutants and lack of appropriate access to health services and screening in developing countries are important points in epidemiological studies of liver cancer in order to identify and control risk factors [13, 16,17].

MATERIALS AND METHODS

Caution must be exercised when interpreting these estimates, given the limited quality and coverage of cancer data worldwide at present, particularly in low- and middle-income countries. IARC's approach is not only to evaluate, compile, and use the data from the Agency's collaborators in these estimates, but also to work alongside national staff to improve local data quality, registry coverage, and analytical capacity. The clear need for investment in population-based cancer registration in low- and middle-income countries led to the launch of the Global Initiative for Cancer Registry Development (GICR), coordinated by IARC. The goal of the GICR is to inform cancer control through defined improvements in the coverage, quality, and use of population-based cancer registration data worldwide. A summary of the steps used to generate the current set of cancer incidence, mortality, and prevalence estimates is provided below. The methods of estimation are country-specific, and the quality of the national estimates depends on the coverage, accuracy, and timeliness of the recorded incidence and mortality data in a given country.

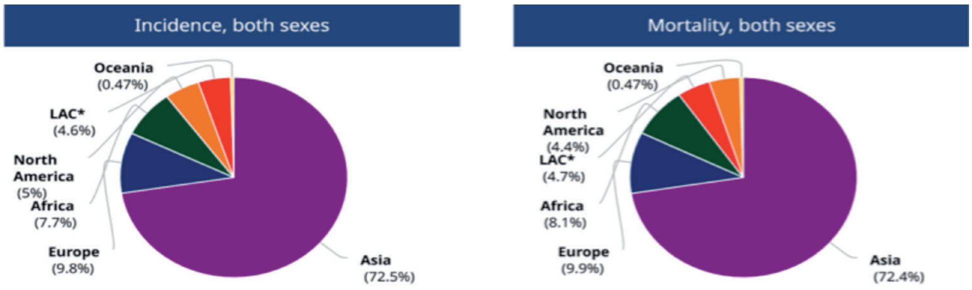
INCIDENCE

The methods used to estimate the sex- and age-specific incidence rates of cancer in a specific country fall into the following broad categories, in order of priority: 1. Observed national incidence rates were projected to 2018 (45 countries). 2. The most recently observed incidence rates (national or regional) were applied to the 2018 population (50 countries). 3. Rates were estimated from national mortality data by modeling, using mortality-to-incidence ratios derived from cancer registries in that country (14 countries). 4. Rates were estimated from national mortality estimates by modeling, using mortality-to-incidence ratios derived from cancer registries in neighboring countries (37 countries). 5. Age- and sex-specific national incidence rates for all cancers combined were obtained by averaging overall rates from neighboring countries. These rates were then partitioned to obtain the national incidence for specific sites using available cancer-specific relative frequency data (7 countries). 6. Rates were estimated as an average of those from selected neighboring countries (32 countries).

MORTALITY

The methods used to estimate the sex- and age-specific mortality rates of cancer in a specific country fall into the following broad categories, in order of priority:

1. Observed national mortality rates were projected to 2018 (81 countries).
2. The most recently observed national mortality rates were applied to the 2018 population (20 countries).
3. Rates were estimated from the corresponding national incidence estimates by modeling, using incidence-to-mortality ratios derived from cancer registries in neighboring countries (81 countries).
4. Rates were estimated as an average of those from selected neighboring countries (3 countries)[18, 19].



Population	Number
Asia	609 596
Europe	82 466
Africa	64 779
North America	41 851
*Latin America and the Carribean	38 400
Oceania	3 988
Total	841 080

Population	Number
Asia	566 269
Europe	77 375
Africa	63 562
*Latin America and the Carribean	36 436
North America	34 339
Oceania	3 650
Total	781 631

Fig. 1. Pie charts present the distribution of cases and deaths by continent in 2018 for both sexes [Source: GLOBOCAN 2018].

HDI

HDI is a compound index of indices in three dimensions: life expectancy, degree of studies, and dominance over required sources for a proper sensible life. All the groups and regions, which have had a remarkable progress in all HDI components, have developed more rapidly in comparison with low or moderate HDI countries. This index means the world is unequal because national average hides most of the different experiences in human's life. There are a lot of inequalities in northern and southern countries. Income inequality has risen inside every country and also between many countries[20-22].

FINDINGS

Based on the results of cancer recordings in 2018, 18078957 cases of cancer were recorded in both genders, 841080 cases (4.7% of all cancers) were related to liver cancer. The highest incidence of liver cancer in the Asian continent was 609596 (72.5%) and the lowest incidence was related to the Oceania continent with 3988 men (0.47%). The number of deaths due to the total cancer in 2018 was 9555027, of which 781631 cases are related to liver cancer. The highest rate of mortality was related to the Asia continent with 566269 cases (72.4%) and the lowest mortality rate was on the Oceania continent with 3650 cases (0.47%) (Figure 1).

According to cancer record results in 2018, 596574 cases of liver cancer in men and 244506 cases were recorded in women, the highest incidence of liver cancer in men in Eastern Asia (26.8 per 100,000) and the lowest incidence in men related to South-central Asia (3.4 in 100,000) was the highest incidence in Melanesia women (8.9 per 1,000,000), and the lowest in South-central Asia (1.7 per 100,000) (Figure 2).

Table 1 shows the incidence and mortality rate of liver cancer worldwide. The results of the study showed that the highest incidence and mortality of liver cancer was in Mongolia and Egypt, with an

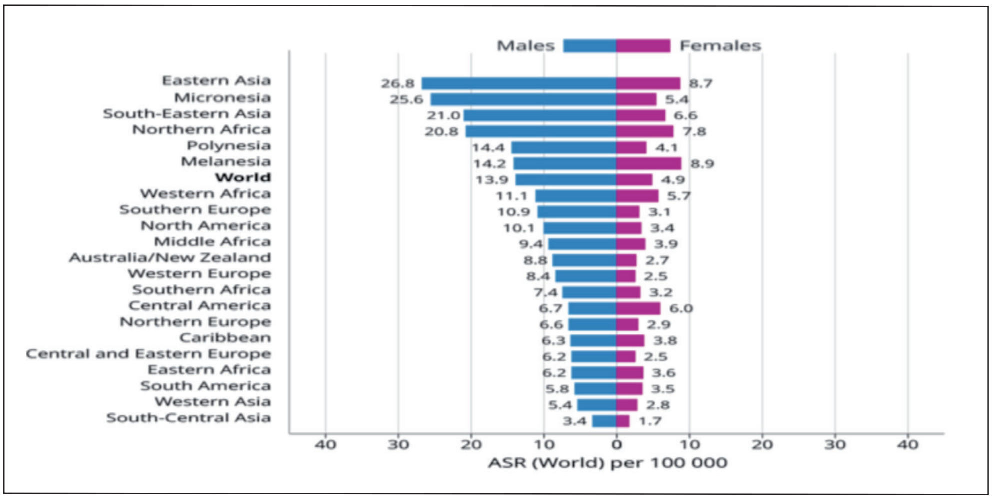


Fig. 2. Bar chart of region-specific incidence and mortality age-standardized rates liver cancer by world area for males and females in 2018 [Source: GLOBOCAN 2018].

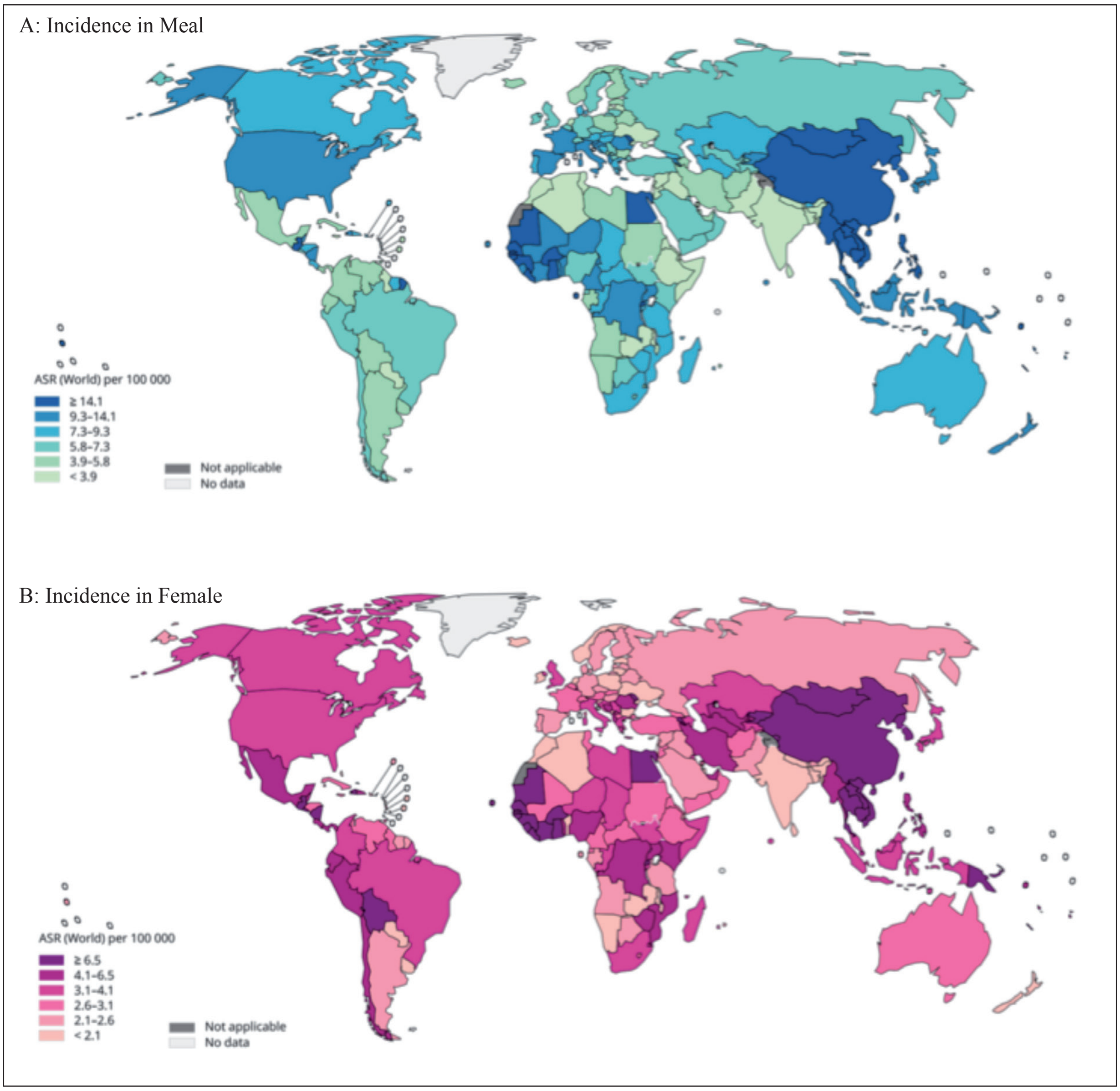


Fig. 3. Global map presenting age-standardized incidence rates liver cancer by world countries for *(A)* males and *(B)* females for all ages in 2018 [Source: GLOBOCAN 2018].

incidence rate in Mongolia (93.7% in 100,000) and in Egypt (32.2 in 100,000), and mortality rate in Mongolia (75.4 per 100,000) and in Egypt (31.8 per 100,000) (Table 1, Figure 4).

Based on the results of cancer registrations in 2018, the highest incidence (13.8 per 1000000) and mortality (13 per 100,000) are related to high HDI areas (Figure 5).

The results of analysis of variance showed that the highest average rate of liver cancer was related to medium human development (8.3 out of 100,000) and the lowest mean incidence (5.3 out of 100,000) was related to very high human development, but this difference was not statistically significant (p>0.05). The lowest mortality rate (4.5 out of 100,000) was related to very high human development and the highest (8.2 out of 100,000) was related to medium human development, but this difference was not statistically significant (p>0.05) (Table 2)

The results showed that there was a negative correlation between incidence and mortality of liver cancer and HDI index. This correlation was not significant between the incidence of liver cancer and HDI index (r=-0.09, p>0.05), while the correlation between liver cancer mortality and HDI index (r=-0.149, p<0.05) was statistically significant such as that with increasing HDI, mortality decreases (Figure 6).

R Sq. linear=--0.149, p<0.05
R Sq. linear=--0.09, p>0.05

TABLE 1. Estimated age-standardized incidence and mortality rates liver cancer, both sexes, all ages in World in 2018.

	Incidence			Mortality			
	Crud Rate	ASR	Cum. Risk	Crud Rate	ASR	Cum. Risk	HDI
Afghanistan	1.8	3.9	0.46	1.7	3.8	0.45	0.479
Albania	14.8	7.8	0.84	14.7	7.6	0.81	0.764
Algeria	1.3	1.4	0.17	1.3	1.4	0.16	0.745
Angola	1.9	3.6	0.41	1.8	3.5	0.39	0.533
Argentina	5.2	3.6	0.43	4.7	3.2	0.38	0.827
Armenia	16.2	9.7	1.1	15.5	9.4	1.1	0.743
Australia	9.8	5.7	0.67	9.5	4.8	0.56	0.939
Austria	12.8	5.4	0.67	10.8	4.3	0.53	0.893
Azerbaijan	3.9	3.6	0.45	3.8	3.5	0.44	0.759
Bahamas	3.5	2.3	0.26	3.5	2.3	0.26	0.792
Bahrain	1.9	3.4	0.37	1.8	3.3	0.36	0.824
Bangladesh	1.9	2.2	0.24	1.7	2	0.24	0.579
Barbados	4.9	2.4	0.26	4.9	2.4	0.26	0.795
Belarus	5.9	3.3	0.39	4	2.2	0.27	0.796
Belgium	8.7	4.3	0.55	8.7	3.6	0.42	0.896
Belize	5	8.4	1	5	8.4	1	0.706
Benin	2.6	5.1	0.42	2.7	5.3	0.44	0.485
Bhutan	4.3	5.3	0.66	4	5.1	0.65	0.607
Bolivia, Plurinational State of	6	6.1	0.64	5.9	6	0.62	0.674
Bosnia and Herzegovina	15.8	7.4	0.96	15	6.4	0.71	0.75
Botswana	2.7	3.9	0.39	2.6	3.8	0.38	0.698
Brazil	5.9	4.7	0.54	5.6	4.4	0.51	0.754
Brunei	8.8	9.9	1.2	7.1	8.3	0.95	0.865
Bulgaria	7.9	3.6	0.43	8.3	3.6	0.43	0.794
Burkina Faso	6.6	13.8	1.6	6.4	13.5	1.6	0.402
Burundi	3.6	6.3	0.67	3.6	6.6	0.7	0.404
Cabo Verde	8	10.7	1.3	8.5	11.2	1.3	0.648
Cambodia	15.7	21.8	2.6	15.7	21.9	2.6	0.563
Cameroon	3.9	6.1	0.58	3.6	6	0.57	0.518
Canada	10.5	5.3	0.64	10.4	4.5	0.53	0.92
Central African Republic	3.1	5.1	0.52	2.8	4.8	0.5	0.352
Chad	2.6	5.5	0.59	2.4	5.3	0.57	0.396
Chile	8.7	5.4	0.64	8	4.9	0.58	0.847
China	27.6	18.3	2.1	25.9	17.1	1.9	0.738
Colombia	4.6	3.9	0.43	4.5	3.8	0.42	0.727
Comoros	3.5	5.7	0.69	3.4	5.8	0.7	0.497
Congo, Democratic Republic of	4.3	8	0.86	4.3	8.1	0.88	0.435
Congo, Republic of	3.8	5.9	0.59	3.4	5.4	0.56	—
Costa Rica	8.6	6.3	0.71	8	5.6	0.61	0.776
Croatia	15.3	6.3	0.75	13.1	5.2	0.63	0.827
Cuba	7.3	3.8	0.44	6.7	3.3	0.39	0.775
Cyprus	6.3	3.4	0.4	8.5	4.6	0.51	0.856
Czech Republic	10	4.2	0.53	8.2	3.2	0.41	0.878
Côte d'Ivoire	4.5	8.4	0.98	4.5	8.4	0.98	0.474
Denmark	10.6	4.9	0.62	10.1	4.2	0.51	0.925
Djibouti	2	2.6	0.33	1.8	2.4	0.32	0.473
Dominican Republic	6.6	6.5	0.77	6	5.8	0.68	0.726
Ecuador	5.8	5.3	0.54	5.7	5.1	0.52	0.739
Egypt	25.6	32.2	3.8	25.2	31.8	3.8	0.691
El Salvador	8	6.7	0.71	7.8	6.5	0.69	0.68
Equatorial Guinea	3.3	4.7	0.5	3.2	4.9	0.52	0.592

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TABLE 1 (CONTINUED). Estimated age-standardized incidence and mortality rates liver cancer, both sexes, all ages in World in 2018.

	Incidence			Mortality			
	Crud Rate	ASR	Cum. Risk	Crud Rate	ASR	Cum. Risk	HDI
Eritrea	1.8	3.3	0.37	1.7	3.2	0.38	0.42
Estonia	7.9	3.2	0.4	7.3	2.9	0.36	0.865
Ethiopia	1.5	2.7	0.3	1.5	2.7	0.31	0.448
Fiji	8.3	8.3	0.96	8.2	8.2	0.95	0.736
Finland	9.9	3.6	0.44	10.4	3.6	0.43	0.895
France	16.3	7.8	0.96	15.4	6.3	0.74	0.897
France, Guadeloupe	7.6	3.7	0.41	6.7	2.6	0.27	—
France, La Réunion	9.6	6	0.71	10.1	6.1	0.75	—
France, Martinique	10.1	4.1	0.41	9.9	3.8	0.43	—
France, New Caledonia	13.6	10.4	1.2	9.3	6.8	0.92	—
French Guyana	7.2	8.5	1.1	4.1	4.9	0.59	—
French Polynesia	11.9	9.5	1	11.9	9.5	1	
Gabon	2.7	3.3	0.35	2.5	3.3	0.35	0.697
The Gambia	14.7	23.9	2.4	15.9	26.2	2.6	—
Gaza Strip and West Bank	0.93	1.8	0.2	0.89	1.8	0.2	—
Georgia	9.7	5.4	0.62	9.5	5.2	0.6	0.769
Germany	10.8	4.2	0.52	10.5	3.8	0.46	0.926
Ghana	9.3	15.4	1.7	9.3	15.4	1.7	0.579
Greece	14.7	5.7	0.68	13.3	4.5	0.5	0.866
Guam	18.7	14.8	1.8	15.1	11.9	1.5	—
Guatemala	10.4	14.9	1.7	10.1	14.5	1.7	0.64
Guinea	12.1	21.8	2.6	10.8	19.5	2.3	0.414
Guinea-Bissau	6.6	11.9	1.4	6.7	12	1.4	0.424
Guyana	2.6	2.7	0.35	2.6	2.8	0.35	0.638
Haiti	6	8.1	0.92	5.9	7.8	0.86	0.493
Honduras	4.3	5.7	0.65	4	5.4	0.61	0.625
Hungary	11.2	5.4	0.66	9.5	4.4	0.54	0.836
Iceland	4.4	2.5	0.33	7.1	3.5	0.4	0.921
India	2	2.2	0.26	1.9	2	0.25	0.624
Indonesia	6.9	7.6	0.88	6.8	7.5	0.87	0.689
Iran, Islamic Republic of	4.3	4.7	0.48	4.2	4.7	0.48	0.774
Iraq	1.4	2.7	0.32	1.4	2.7	0.32	0.649
Ireland	7.6	4.3	0.52	7.9	4	0.44	0.923
Israel	4	2.6	0.28	4.7	3	0.35	0.899
Italy	20.8	7.9	0.94	17.8	5.7	0.64	0.887
Jamaica	3.7	2.9	0.34	3.6	2.7	0.31	0.73
Japan	27.9	7.6	0.82	22.8	5.4	0.53	0.903
Jordan	1.9	3.1	0.31	1.8	2.9	0.3	0.741
Kazakhstan	6.1	5.6	0.71	5.4	5	0.66	0.794
Kenya	2.6	5.3	0.65	2.6	5.3	0.65	0.555
Korea, Democratic Republic of	22.3	16.5	1.9	20.5	15	1.7	—
Korea, Republic of	32.3	17.3	2.1	23.7	11.8	1.3	0.901
Kuwait	2.9	5.2	0.6	2.7	5	0.6	0.8
Kyrgyzstan	7.4	9.5	1.2	6.8	8.7	1.1	0.664
Lao People’s Democratic Republic	14.9	22.4	2.7	14.8	22.4	2.7	0.586
Latvia	7.9	3.1	0.38	7.2	3.1	0.37	0.83
Lebanon	3.7	3.2	0.38	3.5	3	0.37	0.763
Lesotho	3	4.4	0.4	3	4.4	0.39	0.497
Liberia	8.5	15.2	1.8	8.7	15.4	1.8	0.427
Libya	3	4.1	0.54	2.3	3.3	0.44	0.716
Lithuania	8.6	3.8	0.47	7.7	3.3	0.4	0.848

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TABLE 1 (CONTINUED). Estimated age-standardized incidence and mortality rates liver cancer, both sexes, all ages in World in 2018.

	Incidence			*Mortality*			
	Crud Rate	*ASR*	*Cum. Risk*	*Crud Rate*	*ASR*	*Cum. Risk*	*HDI*
Luxembourg	11.9	6.5	0.83	9	4.4	0.48	0.898
Madagascar	3.4	5.8	0.62	3.5	6	0.64	0.512
Malawi	1.5	2.1	0.19	1.6	2.5	0.23	0.476
Malaysia	6.1	6.3	0.74	6	6.3	0.73	0.789
Maldives	6.1	8.3	1	5.9	8.2	1	0.701
Mali	3.1	6.3	0.68	2.9	5.9	0.65	0.442
Malta	5.1	2.2	0.24	5.6	2.4	0.25	0.856
Mauritania	7	11.3	1.3	7.2	11.5	1.3	0.513
Mauritius	5	3.2	0.43	4.2	2.7	0.31	0.781
Mexico	5.6	5.4	0.63	5.3	5.1	0.6	0.762
Mongolia	71.8	93.7	10.8	56.8	75.4	8.7	0.735
Montenegro	8.3	3.9	0.42	8.3	3.9	0.42	0.807
Morocco	1.2	1.1	0.14	1.1	1.1	0.13	0.647
Mozambique	3.9	6.6	0.67	3.8	6.7	0.68	0.418
Myanmar	9.8	10.1	1.2	10	10.1	1.2	0.556
Namibia	1.9	2.8	0.35	1.8	2.9	0.36	0.64
Nepal	0.95	1.1	0.12	0.88	1	0.12	0.558
New Zealand	10.2	5.8	0.69	7.4	3.9	0.46	0.915
Nicaragua	9	10.5	1.3	8.5	9.9	1.2	0.645
Niger	3.5	7.3	0.83	3.4	7.2	0.82	0.353
Nigeria	2.6	5.1	0.54	2.6	5.1	0.55	0.527
Norway	6.2	3.4	0.4	6.1	2.9	0.33	0.949
Oman	2.4	4.4	0.51	2.3	4.3	0.5	0.796
Pakistan	2.2	3.1	0.36	2.1	3	0.36	0.55
Panama	6	4.8	0.52	5.7	4.6	0.51	0.788
Papua New Guinea	8.7	11.9	1.3	7.5	10.9	1.2	0.516
Paraguay	2.6	2.8	0.33	2.6	2.9	0.33	0.693
Peru	7.1	6.6	0.73	6.9	6.3	0.7	0.74
Philippines	9	11.5	1.3	8.9	11.4	1.3	0.682
Poland	6.7	3.2	0.37	5.9	2.7	0.31	0.855
Portugal	13.5	5.4	0.63	13.3	5.2	0.61	0.843
Puerto Rico	9.6	5.2	0.62	10.2	5.3	0.64	---
Qatar	1.6	4.1	0.45	1.5	4	0.44	0.856
Republic of Moldova	21.1	13.8	1.7	17.3	11.2	1.4	---
Romania	17.6	8.4	1	16	7.5	0.93	0.802
Russian Federation	7.2	3.9	0.46	7.8	4.1	0.5	0.804
Rwanda	5.9	10.1	1.1	5.6	10.2	1.1	0.498
Saint Lucia	2.2	1.5	0.2	2.2	1.1	0.05	0.735
Samoa	8.1	9.8	1.2	3.5	4.8	0.8	0.704
Sao Tome and Principe	3.8	8.3	1.3	3.8	8.3	1.3	0.574
Saudi Arabia	2.7	4.5	0.55	2.5	4.2	0.52	0.847
Senegal	6.6	12.6	1.4	6.6	12.6	1.4	0.494
Serbia	8.8	4.4	0.56	10.2	4.7	0.57	0.776
Sierra Leone	5.3	10	1.1	4.8	9.5	1.1	0.42
Singapore	23.8	12.3	1.4	22.4	11.4	1.2	0.925
Slovakia	9.4	5	0.61	8.7	4.3	0.53	0.845
Slovenia	14	5.8	0.73	12.9	5	0.6	0.89
Solomon Islands	6.6	10.3	1.2	8.8	13.7	1.5	0.515
Somalia	1.7	3.4	0.4	1.6	3.3	0.39	—
South Africa	4.3	5	0.55	4.2	4.8	0.52	0.666
South Sudan	3.1	5.1	0.55	3.1	5.2	0.57	0.418

Continued

TABLE 1 (CONTINUED). Estimated age-standardized incidence and mortality rates liver cancer, both sexes, all ages in World in 2018.

	Incidence			*Mortality*			
	Crud Rate	*ASR*	*Cum. Risk*	*Crud Rate*	*ASR*	*Cum. Risk*	*HDI*
Spain	14.3	6.5	0.78	12	4.7	0.54	0.884
Sri Lanka	3.7	2.7	0.3	2.9	2.2	0.26	0.766
Sudan	2.3	3.8	0.43	2.2	3.7	0.43	0.49
Suriname	6	5.6	0.65	7.6	7.1	0.74	0.725
Swaziland	2.7	3.9	0.34	2.5	3.9	0.33	0.541
Sweden	9.8	4.5	0.52	7.9	3.1	0.35	0.913
Switzerland	11.1	4.8	0.6	10.2	4.1	0.48	0.939
Syrian Arab Republic	2.1	3	0.34	2.1	3	0.34	0.536
Tajikistan	3	4.7	0.55	2.8	4.4	0.55	0.627
Tanzania, United Republic of	2.6	4.9	0.56	2.6	5	0.56	0.531
Thailand	33.7	21	2.5	33.5	20.9	2.4	0.74
The Netherlands	5.9	2.5	0.28	6.1	2.5	0.28	—
The former Yugoslav Republic of Macedonia	8.9	5	0.63	9	5	0.63	0.748
Timor-Leste	2.9	5.3	0.63	2.9	5.3	0.63	0.605
Togo	3.9	6.9	0.77	3.9	6.9	0.77	0.487
Trinidad and Tobago	4.8	3.3	0.37	4.6	3.2	0.35	0.78
Tunisia	3	2.6	0.29	3.1	2.6	0.3	0.725
Turkey	5.3	4.5	0.52	5.3	4.4	0.52	0.767
Turkmenistan	4.8	6	0.72	4.5	5.6	0.69	0.691
Uganda	4.1	7.6	0.77	3.5	6.7	0.7	0.493
Ukraine	4.1	2.2	0.27	5.1	2.7	0.32	0.743
United Arab Emirates	1	4.2	0.47	1	4.2	0.45	0.84
United Kingdom	11.4	5.1	0.59	10.3	4	0.44	0.909
United States of America	11.6	6.8	0.82	9.3	4.9	0.6	0.92
Uruguay	4.6	2.6	0.32	3.8	2.1	0.26	0.795
Uzbekistan	4.5	5.6	0.65	3.7	4.7	0.61	0.701
Vanuatu	9.9	13.1	1.5	9.9	13.1	1.5	0.597
Venezuela, Bolivarian Republic of	3.7	3.6	0.4	3.6	3.5	0.38	0.767
Viet Nam	26.3	23.2	2.6	26.3	23.2	2.6	0.683
Yemen	2.1	4.4	0.51	2.1	4.3	0.51	0.482
Zambia	1.1	2.2	0.27	0.98	2.1	0.25	0.579
Zimbabwe	3.4	6.9	0.75	3.4	0.7	0.75	0.516

The results showed that there was a negative correlation between the incidence of liver cancer with GNI, MYS, LEB and EYS, which was not statistically significant ($p > 0.05$). The results also showed a negative and significant correlation between mortality rate and MYS ($r = -0.154$, $p < 0.05$) (Table 3).

DISCUSSION

Gastrointestinal cancers, including liver cancer, account for a major proportion of the burden of diseases, and since this cancer is detected at advanced stages of the disease, it has many complications that affect all body parts[1,23]. In this study in 2018, the number of new cases of liver cancer was 18078957 and the number of deaths from this cancer was 841080 cases (4.7% of all cancers). The highest incidence and mortality of liver cancer was in Asia and in the countries of Mongolia and Egypt. The results showed a negative correlation between incidence of liver cancer and HDI index, but this correlation was not significant. However, there was a negative and significant correlation between liver cancer mortality and HDI index. There was also a negative correlation between the incidence of liver cancer with GNI, MYS, LEB and EYS, which was not statistically significant, but correlation between mortality rate and MYS was significant.

Findings from a study by Njei et al[24] conducted on data from incidence and mortality rates during 1973-2011 in the United States showed that incidence rate of liver cancer was 1.51 cases per 100000 in 1973, while in 2011 it was reported to be 6.2 cases per 100000.

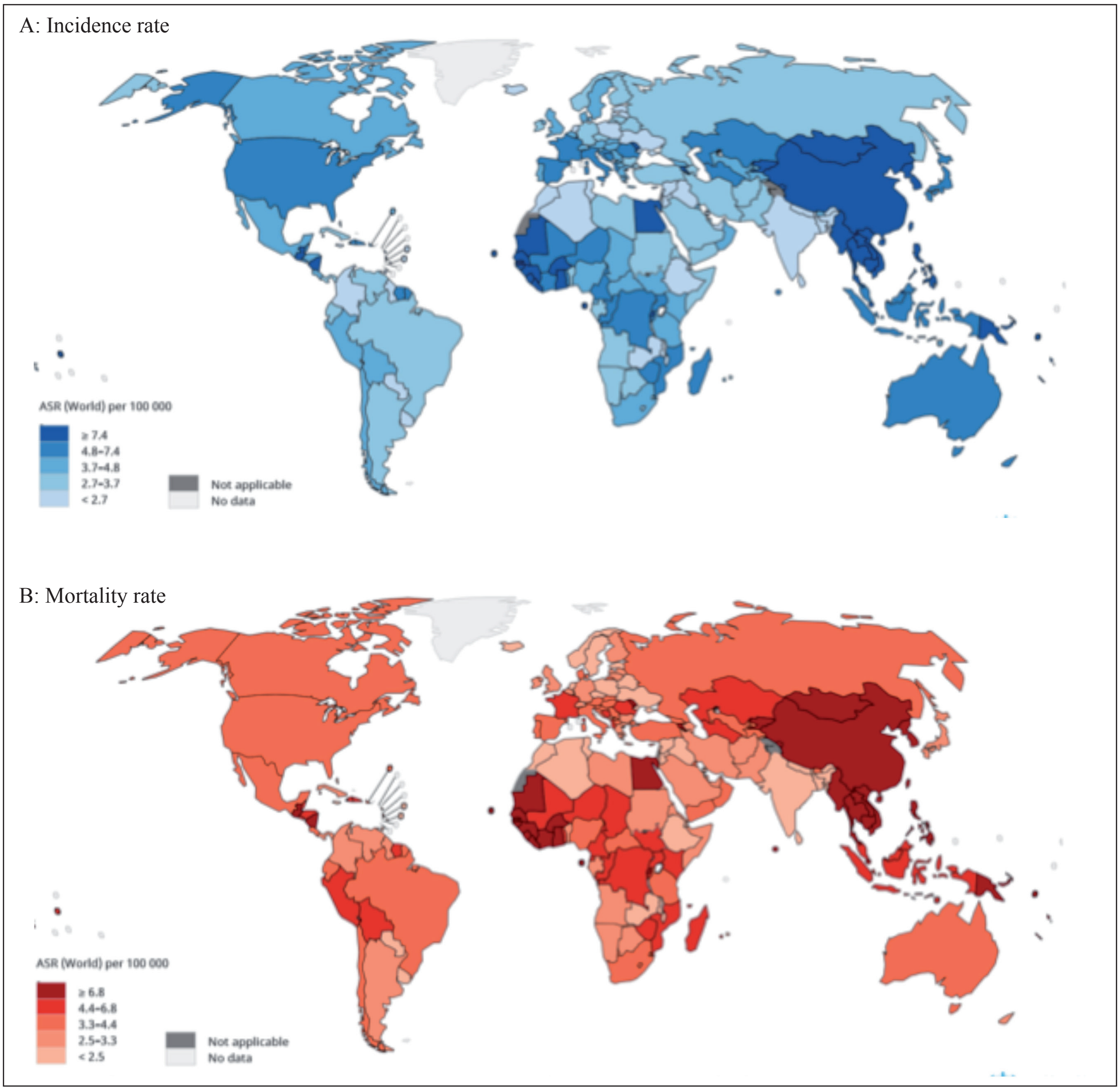

Fig. 4. Global map presenting age-standardized *(A)* incidence and *(B)*mortality rates liver cancer by world countries for both sexes all age in 2018 [Source: GLOBOCAN 2018].

Ascione et al[25] in their study, using recorded death data due to liver cancer from 1970 to 2010, reported that the highest mortality rate due to liver cancer was related to Portugal, followed by France and Italy in 1970. Also, in 2010, 3 countries with the highest deaths rate due to liver cancer were Finland, Austria and Germany.

Results of a study by Beal et al[26] demonstrated that mortality rate of liver cancer has increased from 9.2 cases per 100,000 in 1999 to 14.6 per 100,000 in 2015. In women mortality rate has also increased from 2.9 to 3.3 per 100,000. In this study, the highest mortality rate was observed in men aged 70 and older, although the highest mortality rate was observed during 1999-2015 in men aged 55-69.

In 2012 there were 782,000 new cases of liver cancer in the worldwide, associated with 746,000 deaths. Therefore, this cancer is the fifth most common cancer in men (7.5% of all cancers) and the ninth common cancer among women (3.4% of all cancers). The incidence of LC and its mortality rate has been considerably concentrated in moderate and low HDI areas. There was a negative and significant correlation between the incidence and mortality rate of LC with HDI. As this index increases, the incidence and mortality rate of the LC significantly decreases. The negative relationship between each of the main components of HDI and other indicators, including urbanization and obesity in adulthood was significant. But there was not significant negative relationship between life expectancy and LC death[17] .

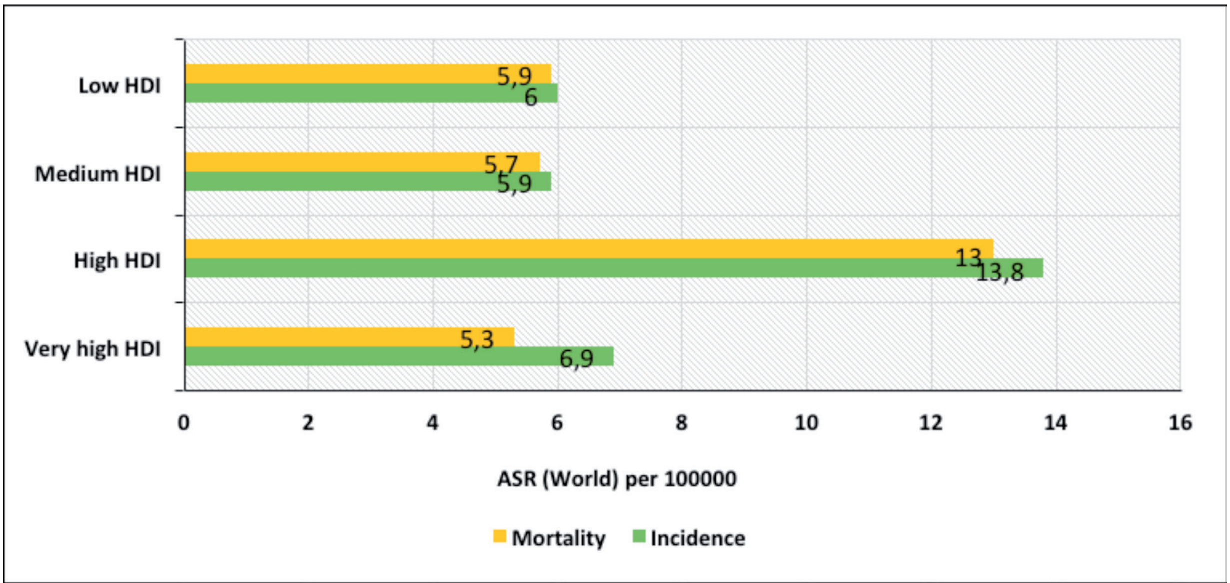

Fig. 5. Distribution of liver cancer based HDI.

In 2012 a total of 782451 new cases of liver cancer and 745533 related deaths were recorded. The highest incidence of liver cancer in both sexes and the highest mortality rate among women in the world were seen in the countries of East Asia, and North Africa. The highest rates of liver cancer deaths in men were reported in the countries of East Asia, West Africa and Melanesia. Approximately 95% of all incidence and 96% of LC deaths occurred in less developed areas. Findings suggest that countries with higher levels of HDI and GDP were associated with a lower incidence and mortality rate of liver cancer[16] .

In 2012 a total of 782451 new cases of the disease were reported, of which 554,369 were male (70.85%) and 228082 (29.15%) were female. Also, the number of death from this cancer was 745,533 people, 69.89% in men and 30.11% in women, among the countries of the world, the highest incidence was related to Mangulia and the lowest incidence was related to Nepal. There was a significant and inverse correlation between mortality rates of LC and HDI. The rate of liver cancer and its mortality was higher in countries with moderate HDI. This association was between standardized incidence and death of liver cancer with HDI and its components, including life expectancy at birth, average years of education, and income was negative. The lowest incidence of LC was also found in areas with high human development[27] .

The hepatocyte carcinoma (HCC) has a global importance due to its high rate of progression and high mortality rates[12]. Almost 85% of LC incidence and mortality cases occur in developing countries and significantly in countries with low and moderate HDIs. It can be said that these countries are often in the process of industrialization, and this affects all aspects of their lives, including those related to health[17]. In countries with low and medium HDI, HCC risk factors, including diabetes 36, metabolic syndrome 37, obesity 38, alcoholic beverages 39, HBV and HCV infection has a higher incidence[16].

According to World Health Organization (WHO), nearly 2 billion people in the world have serologic evidence of hepatitis B virus infection of these, 360 million people are infected with chronic HBV infection (chronic carriers). Chronic carriers with complications

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

	Incidence Rate		*Mortality Rate*	
	CR	***ASR***	***CR***	***ASR***
Very high human development	10.4	5.3	9.5	4.5
High human development	8.2	7.1	7.6	6.4
Medium human development	6.5	8.3	6.4	8.2
Low human development	4.1	7.2	4	6.9
***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.

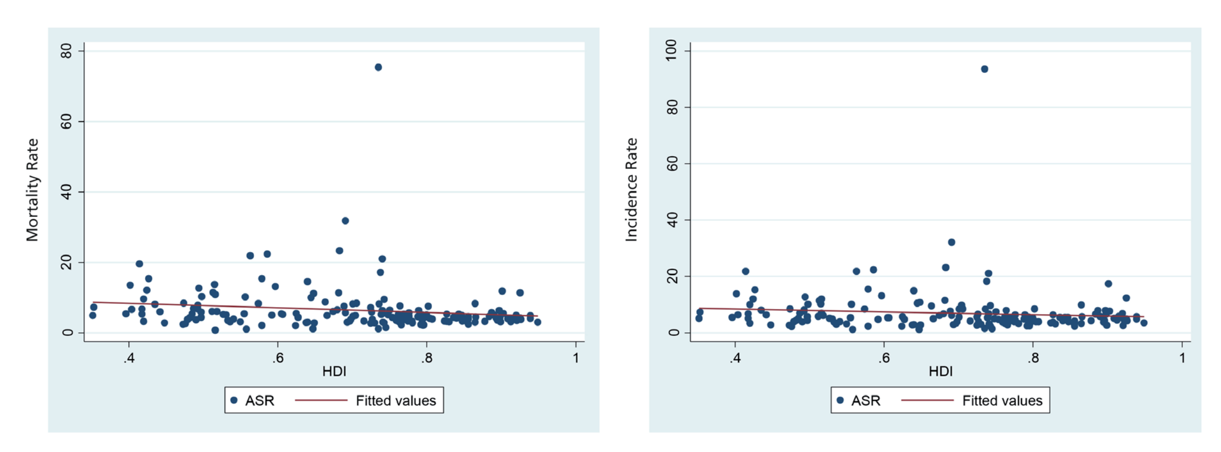

Fig. 6. Correlation between HDI, incidence and mortality rates of cancer liver in world in 2018.

such as cirrhosis or liver failure, hepatocellular carcinoma, and death will struggle. The annual mortality rate associated with HBV infection is reported to be between 500,000-700,000 cases. Nearly 60 percent of the world's populations live in hepatitis B hyper-endemic countries, such as China, Taiwan, Indonesia, and some Asian-African countries[28, 29]. Therefore, the prevention of hepatitis B incidence in infants and children is the most important factor in preventing hepatitis B and its progress towards cirrhosis and liver failure and hepatocellular carcinoma.

The negative relationship between the incidence and death due to LC with HDI and its components has been agreed in the most studies, which can be considered as one of the most important goals in the field of prevention and treatment. The average increase in academic years as one of the most important health indicators varies widely between different countries and regions[17]. In high-HDI societies, people are less likely to be exposed to risk factors due to an increase in their average academic years, and are more likely to have contact with care systems, resulting in less LCs incidence and death[27]. On the other hand, the incidence and mortality rate of liver cancer in countries with high prevalence, including Japan and China, is declining. One of the main reasons is the reduction of aflatoxin contamination, immunization against HBV and other cancer prevention programs. Reduction of chronic schistosomiasis infection, more health measures in the transmission and donation of blood to prevent HCV infection, implementation of policies to prevent unnecessary intravenous infusion has also been effective. Other preventive strategies in some countries are lifestyle changes (such as avoiding smoking and alcohol consumption), preventing water source pollution, using sterile needles in intravenous drug users, preventing contamination of products with aflatoxin and improve medical interventions (new antiviral treatments)[16] .

CONCLUSIONS

Liver cancer (LC) is one of the most common malignancies, which is significantly increasing in men than women. Considering that the highest incidence and mortality of liver cancer is related to the Asian continent and there is a negative correlation between the developmental index and the incidence and mortality of the disease therefore, consideration of the developmental index and the change of liver cancer risk factors, and especially the screening of people with hepatitis B and C in the continents of Asia, can be effective in reducing the incidence and mortality of the disease.

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

	ASIR*		ASMR*	
	r	*p-value*	*r*	*p-value*
Gross national income per 1000 capita	-0.101	$p>0.05$	-0.14	$p>0.05$
Mean years of schooling	-0.09	$p>0.05$	-0.154	$p>0.05$
Life expectancy at birth	-0.07	$p>0.05$	-0.108	$p>0.05$
Expected years of schooling	-0.07	$p>0.05$	-0.106	$p>0.05$

*Dependent variables: ASIR and ASMR.

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Authors' contribution

E G, A MJ data collection. SLD, F GH, ZK H and HA A analyzed data, and MS, Z KH, E G and HA A interpreted data. Z KH, E G, M S and A MJ drafted the initial manuscript. Z KH, E G and A MJ were major contributors in writing the manuscript, with critical revisions from Z KH, EG and H AA. All authors read and reviewed the final manuscript.

Conflict of Interest

The authors declare no conflict of interest.

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