World Cancer Research Journal WCRJ 2019; 6: e1433

WORLDWIDE INCIDENCE AND MORTALITY OF COLORECTAL CANCER AND HUMAN DEVELOPMENT INDEX (HDI): AN ECOLOGICAL STUDY

E. GOODARZI[1], R. BEIRANVAND[2], H. NAEMI[3], V. MOMENABADI[4], Z. KHAZAEI[5]

[1]Social Determinants of Health Research Center, Lorestan University of Medical Sciences, Khorramabad, Iran
[2]School of Medicine, Dezful University of Medical Sciences, Dezful, Iran
[3]Iranian Research Center on Healthy Aging, Sabzevar University of Medical Sciences, Sabzevar, Iran
[4]Department of Health Education and Health Promotion, School of Health, Shiraz University of Medical Sciences, Shiraz, Iran
[5]Department of Epidemiology, School of Public Health, Ilam University of Medical Sciences, Ilam, Iran

Abstract – *Objective:* *The aim of this study was to investigate the incidence and mortality of colorectal cancer and its relationship with the Human Development Index (HDI) in 2018.*

Materials and Methods: *The present study is a descriptive-analytic study that is based on the extraction of cancer incidence and mortality data from the GLOBOCAN 2018.*

Results: *The results showed that there is a positive and significant correlation between incidence (R=0.722,* p*<0.0001) and mortality (R=0.62,* p*<0.0001) of colorectal cancer with HDI. There was found a positive and significant correlation between the incidence of cancer with GNI (r=0.564,* p*<0.0001), MYS (r=0.732,* p*<0.0001), LEB (r=0.706,* p*<0.0001) and EYS (r=0.754,* p*<0.0001).*

Conclusions: *HDI can be important in reducing the incidence and mortality of colorectal cancer.*

KEYWORDS: *Incidence, Mortality, Colorectal cancer, HDI.*

INTRODUCTION

Colorectal cancer (CRC) is the third most diagnosed cancer and is the fourth leading cause of death worldwide. Around 1.4 million new cases and nearly 700,000 deaths were recorded in 2012 due to colorectal cancer[1]. In most countries, colorectal cancer has increased[2]. Considering the demographic estimates, the global burden of CRC is expected to increase by 60% and reaches more than 2.2 million new cases and 1.1 million deaths by 2030. The distribution of CRC varies across parts of the world; more than two thirds of all cases and about 60% of all deaths occur in countries with high or very high HDI[3]. In the countries of Eastern Europe, Asia and South America with medium HDI, the incidence and mortality of colorectal cancer is increasing. While in the countries of the United States, Australia, New Zealand and several Western European countries with a very high HDI level, the incidence and morbidity of the disease have remained steady[4].

This disease can be considered as indicator of socio-economic development, and in countries undergoing major change in development, their incidence increases with a daily increasing HDI[2]. An increase in prevalence is associated with changes in the generations, diet patterns, obesity and lifestyle factors in developed countries, in which is also observed that mortality increased, although further improvements in survival through adopting best practices for its treatment and management [3,5]. Therefore, the aim of this study is to investigate the epidemiology of incidence and mortality of cancer in 185 countries and its relationship with HDI index in 2018.

Corresponding Author: Zaher Khazaei, MSc in Epidemiology; e-mail: Zaherkhazaei@yahoo.com

MATERIALS AND METHODS

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, were, 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, were, 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)[6,7]

HDI

HDI is a compound index of 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. As showed by HDI, the world is unequal because national average hides most of the different experiences in human's life. There exit a lot of inequalities in northern and southern countries. Income inequality has risen inside every country and also between many countries[8-10].

Statistical analysis

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

RESULTS

Based on the results of cancer recordings in 2018, 18078957 cases of cancer were recorded in both sexes, of which 1849518 (10.2% of all cancers) were related to colorectal cancer. According to the results, 9555027 deaths due to cancer were recorded in 2018, of which 880792 (9.2%) were related to colorectal cancer. Therefore, colorectal cancer was identified as the third most common cancer and the second cause of death due to cancer in 2018 (Figure 1).

The highest incidence of colorectal cancer in the Asia continent was 957896 cases (51.8%) and the lowest incidence was related to the Oceania continent with 22332 cases (1.2%). Also, the highest mortality rate was in Asia with 461422 cases (72.4%) while the lowest was in Oceania with 8066 cases (0.92%) (Figure 2).

Results showed that the highest incidence of colorectal cancer was in male (41.7 per 100,000) and female (32.1 per 100,000) in Australia and New Zealand. The lowest incidence of colorectal cancer in males (1.6 in 100,000) and in female (3.8 out of 100,000) is in South-Central Asia (Figure 4).

Based on the reported results for cancer in 2018, the highest incidence (30.6 per 1,000,000) and mortality (11.1 per 100,000) of colorectal cancer are related to very high HDI areas (Figure 5).

The results of the variance analysis showed that the highest mean incidence (29.4% in 100,000) of colorectal cancer was related to very high HDI and the lowest incidence (6.7 out of 100,000) was related to low HDI. The mean differences were statistically significant ($p<0.0001$). The highest rate of mortality (11.5 out of 100,000) was related to very high HDI and the lowest mortality (5 out of 100,000) of colorec-

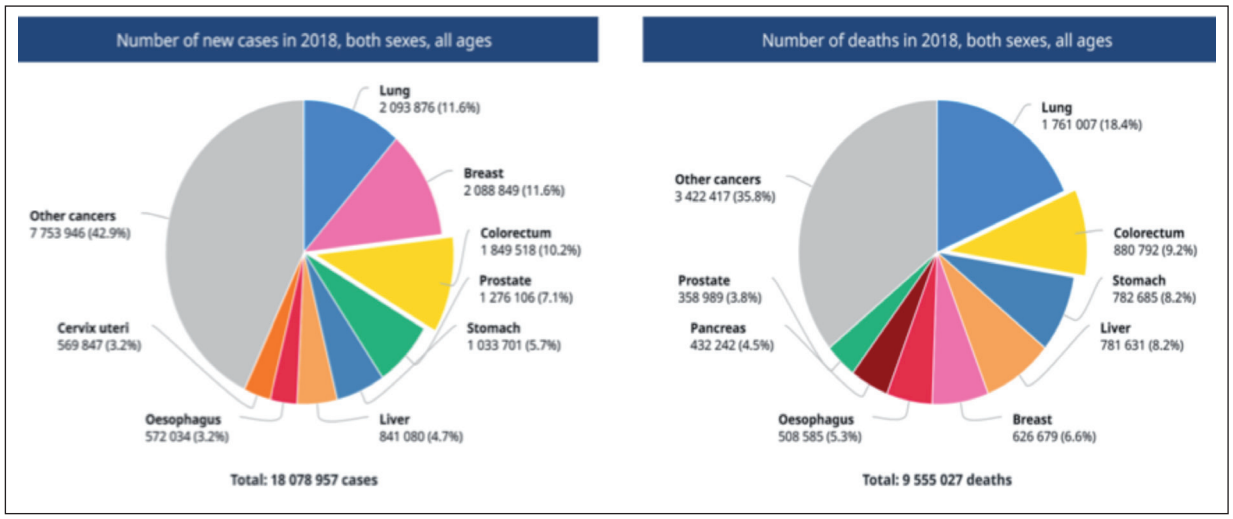


Fig. 1. Pie charts present the distribution of cases and deaths for the 7 most common cancers for both sexes in 2018 in worldwide in all age (source: GLOBOCAN 2018).

tal cancer was related to medium HDI; $p<0.0001$ was considered as statistically significant (Table 1).

The results showed a positive and significant correlation between the incidence rate (R= 0.722, $p<0.0001$) and mortality (R = 0.62, $p<0.0001$) of colorectal cancer with HDI (Figure 6).

The results showed that there is a positive and significant correlation between incidence of cancer with GNI (r=0.564, $p<0.0001$), MYS (r=0.732, $p<0.0001$), LEB (r=0.706, $p<0.0001$) and EYS (r=0.754), $p<0.0001$). Investigating the mortality rate results it was showed a positive and significant correlation between mortality with GNI (r=0.425, $p<0.0001$), MYS (r=0.624, $p<0.0001$), LEB (r=0.579, $p<0.0001$) and EYS r=0.608, $p<0.0001$) (Table 2).

The linear regression model showed that the increase in MYS [B=1.02, CI95% (0.1, 1.8)], EYS [B=1.3, CI 95% (0.3,2.2)] and LBE [B=0.32, CI95% ((0.007,0.6)] significantly increases the incidence of colorectal cancer. In the studying of mortality rate, the results of regression analysis showed that increased MYS [B=0.43, CI 95% (0.07,0.7)] significantly increased mortality rate (Table 3).

DISCUSSION

The relationship between the incidence and mortality of cancers with HDI index was investigated. One of the strongest positive relationships observed

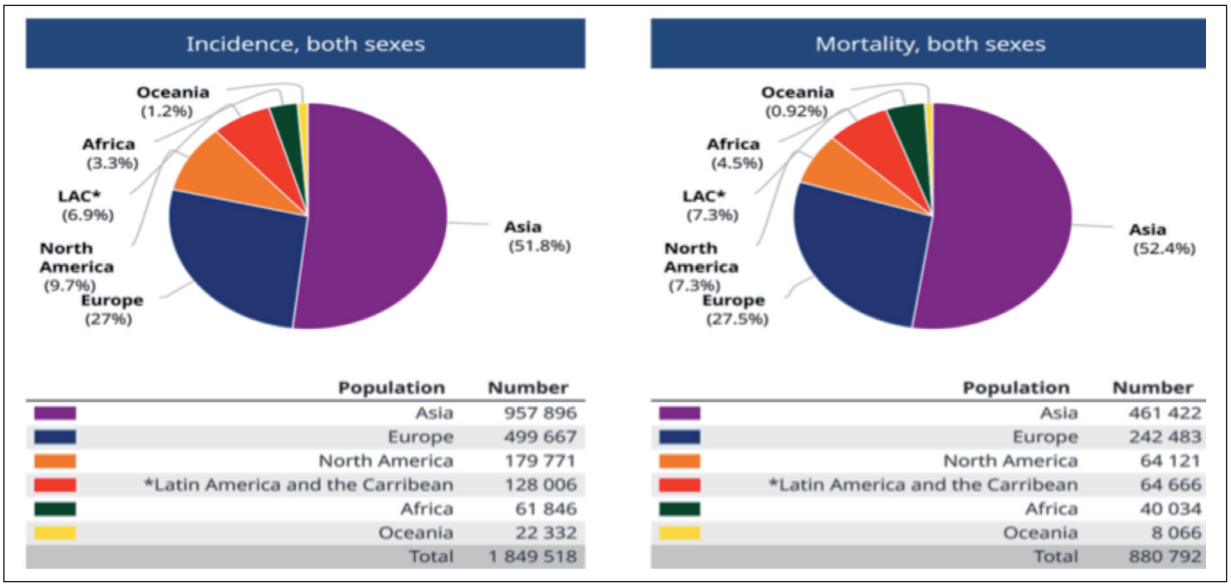


Fig. 2. Pie charts present the distribution of cases and deaths of colorectal cancer by continent in 2018 for both sexes and all age (source: GLOBOCAN 2018).

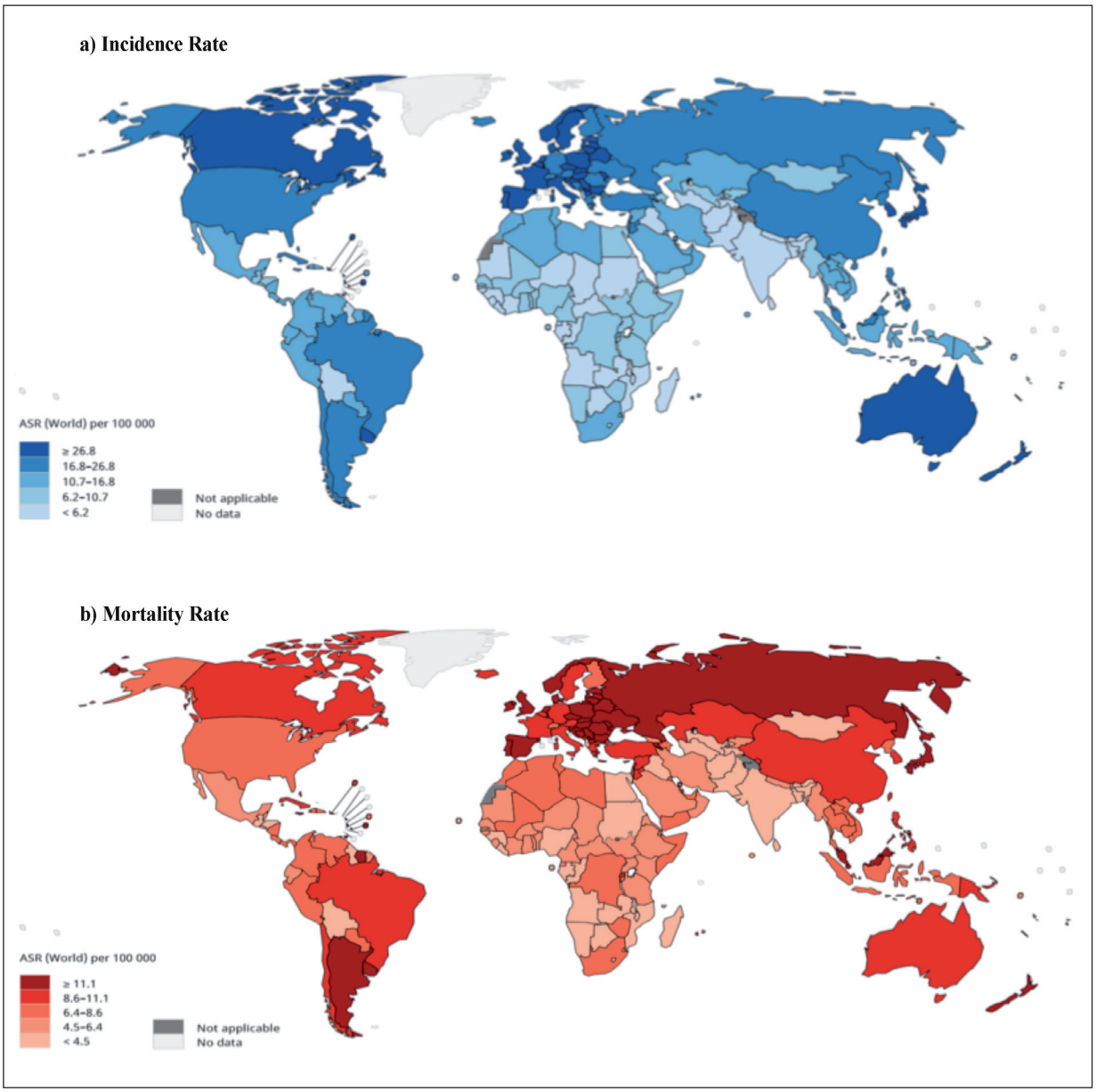


Fig. 3. Global map presenting (a) incidence and (b) mortality rates by world countries for colorectal cancer in both sexes in 2018 (source: GLOBOCAN 2018).

between incidence and HDI index is related to colorectal cancer. Incidence in the very high regions was six to seven times higher than low HDI areas because of lifestyle and environmental changes[2,3,5]. The results of the present study showed that the highest incidence of colorectal cancer in the world was related to the countries of Hungary (51.2 per 100,000), Republic of Korea, (44.5 per 100,000) and Slovakia (43.8 per 100,000). There was a positive and significant correlation between the incidence rate (R=0.722, p<0.0001) and mortality (R=0.62, p<0.0001) of colorectal cancer with HDI index. The linear regression model showed that the increase in MYS [B=1.02, CI95% (0.1, 1.8)], EYS [B=1.3, CI95% (0.3, 2.2)] and LBE [B = 0.32, CI95% ((0.007, 0.6)] significantly increased the incidence of colorectal cancer and the increase in MYS [B=0.43, CI 95% (0.07, 0.7)] significantly raise mortality rate. Different populations around the world have a different incidence rate, and this rate varies over time. In some countries, the incidence rate of the disease has been declining. But in some other regions such as Eastern Europe, it has increased in both sexes[11,12].

The incidence rate of cancer in the high economic levels and high-income countries that have been recently transferred from a low-income economy, such as Japan, Singapore and Eastern European countries, is increasing rapidly[13]. Previous global studies have shown that colorectal cancer is more common in European countries[14].

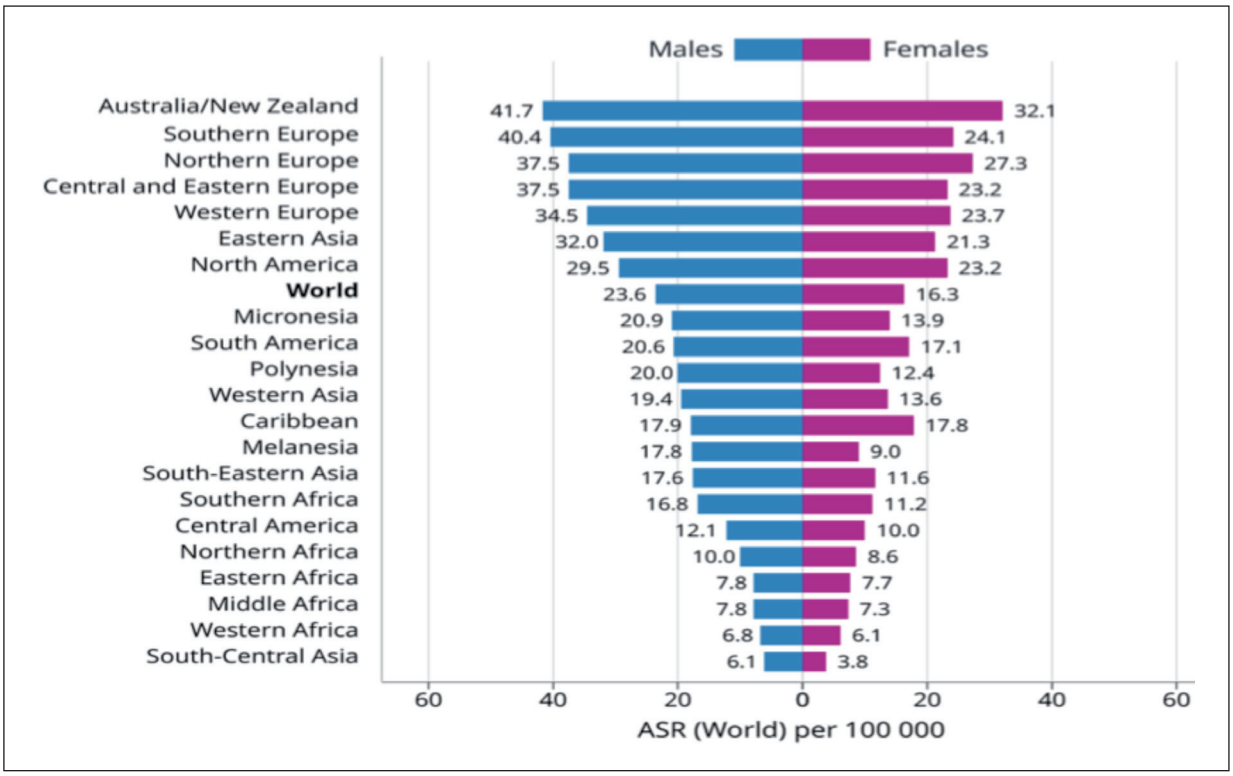
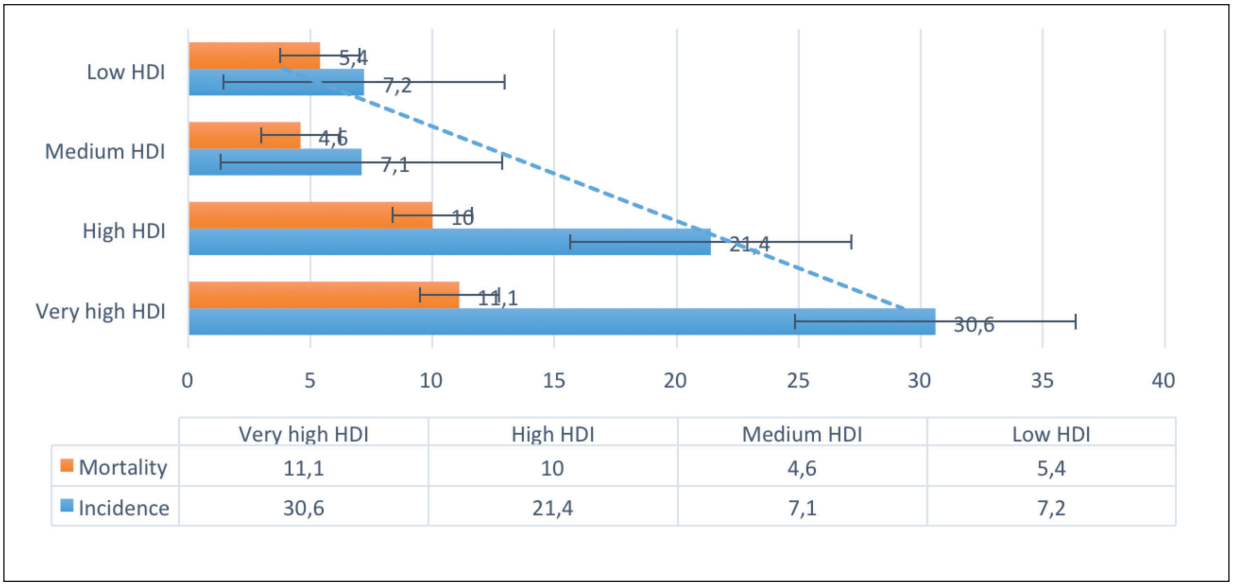


Fig. 4. Bar chart of region-specific incidence rates colorectal cancer by world area for males and female in 2018 (source: GLOBOCAN 2018).

The main reasons for the increase in the incidence rate of colorectal cancer in some regions, such as parts of Asia and Eastern Europe, may be the change in diet, lifestyle changes, and the associated Westernization factors, such as smoking and obesity[15].

Kamangar et al[16] showed that the highest incidence rate of colorectal cancer for both sex was in Oceania, North America and Europe and the standard incidence rate for this cancer in the same period for developed countries was higher than in developing countries.

Various studies have shown that the relationship between risk factors for cancers types and other chronic diseases is illustrated by HDI. Therefore, one of the reasons for the high incidence of colorectal cancer in countries with a high HDI can be



	Very high HDI	High HDI	Medium HDI	Low HDI
Mortality	11,1	10	4,6	5,4
Incidence	30,6	21,4	7,1	7,2

Fig. 5. Distribution of incidence and mortality rates in colorectal cancer by HDI.

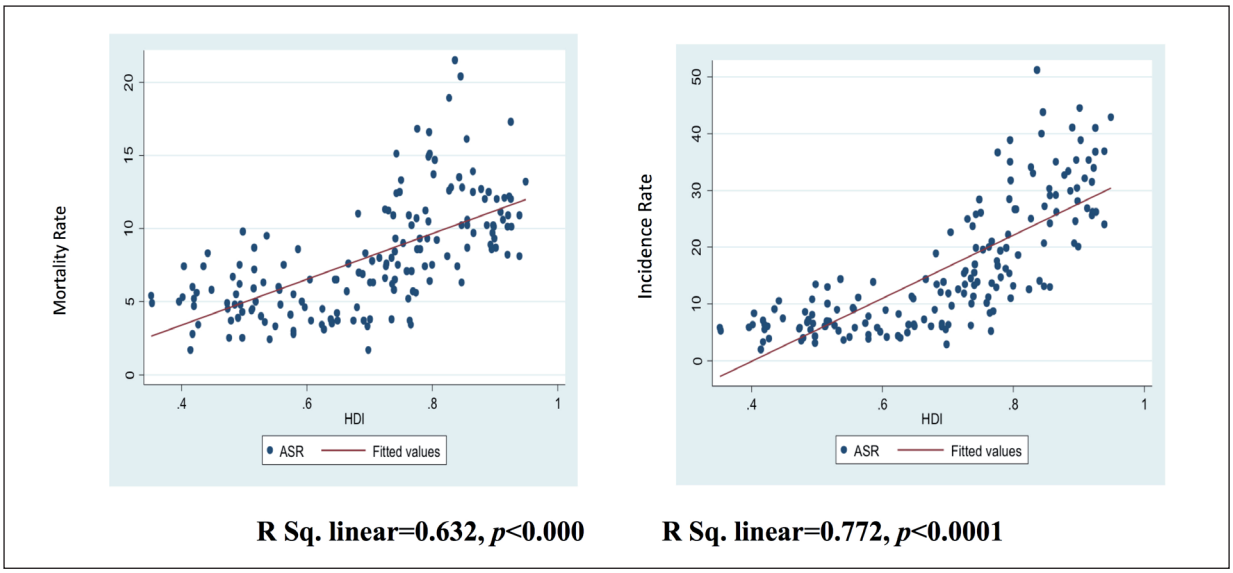


Fig. 6. Correlation between HDI, incidence and mortality rates of colorectal cancer in the world in 2018.

the presence of risk factors for colorectal cancer in these countries[8,17,18]. Colorectal cancer has been the cause of 608700 deaths in 2008 [14]. Studies have shown that deaths from colorectal cancer have declined significantly in some countries, such as North America, New Zealand, Australia and Western Europe. But in some parts of Eastern Europe, deaths have increased from 5% to 15%[19].

In the study of Rafiemanesh et al[20] based on six WHO regions, the highest and lowest mortality rates were in Europe and Africa. The standardized mortality rate, based on the HDI, showed a direct correlation with the highest mortality rates in countries with high rates of HDI. Also, studies carried out worldwide showed the link between cancer deaths (such as breast and bladder cancer) and the HDI[20]. The low mortality rate in countries with low HDI can be for low colorectal cancer due to the lack of proper diagnosis and lack of report and registration of this cancer[21-23]. Another reason for the difference

TABLE 1. Colorectal cancer incidence and mortality in deferent HDI regions in 2018.

	Incidence Rate		*Mortality Rate*	
HDI	***ASR***	***CR***	***ASR***	***CR***
Very high HDI	61.4	29.4	27.1	11.5
High HDI	24.1	17	13	8.8
Medium HDI	6.35	8	3.9	5
Low HDI	3.6	6.7	2.75	5.2
***p*-value (F-test)**	$p<0.0001$	$p<0.0001$	$p<0.0001$	$p<0.0001$

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

TABLE 2. Pearson Correlation between HDI Component and Dependent Variable.

	*ASIR**		*ASMR**	
	r	***p*-value**	***r***	***p*-value**
Gross national income per 1000 capita	0.564	$p<0.0001$	0.425	$p<0.0001$
Mean years of schooling	0.732	$p<0.0001$	0.624	$p<0.0001$
Life expectancy at birth	0.706	$p<0.0001$	0.579	$p<0.0001$
Expected years of schooling	0.754	$p<0.0001$	0.608	$p<0.0001$

*Dependent variables: ASIR and ASMR.

TABLE 3. Effect of HDI components on colorectal cancer incidence and mortality in the world in 2018.

HDI components	*Incidence*			*Mortality*		
	B	*CI 95%*	*p-value*	*B*	*CI 95%*	*p-value*
HDI	-8.5	(-45, 27.9)	$p>0.05$	-1.7	(-17.2, 13.8)	$p>0.05$
Gross national income per 1000 capita	0.007	(-5.8, 0.009)	$p>0.05$	0.008	(-0.002, 0.04)	$p>0.05$
Mean years of schooling	1.02	(0.1, 1.8)	$p>0.05$	0.43	(0.07, 0.7)	$p>0.05$
Life expectancy at birth	0.32	(0.007, 0.6)	$p>0.05$	0.09	(-0.04, 0.2)	$p>0.05$
Expected years of schooling	1.3	(0.3, 2.2)	$p>0.05$	0.24	(-0.1, 0.6)	$p>0.05$

Abbreviations: HDI, Human Development Index; LEB, Life Expectancy at Birth; MYS, Mean Years of Schooling; GNI, Gross National Income per capita, EYS: Expected years of schooling

in the incidence and mortality of colorectal cancer with the country's development index is the existence and use of screening and diagnostic tests such as sigmoidoscopy and colonoscopy[24,25].

Studies have shown that the most important risk factors for colorectal cancer are related to nutritional factors, if lifestyle changes and nutrition are appropriate, 30-50% of cases of colorectal cancer will be prevented[19].

These significant risk factors include alcohol use[26,27], inappropriate diet (low consumption of fruits and vegetables and high consumption of red meat/processed meat)[28,29], obesity[30,31], physical inactivity[32] and cigarettes[33-35]. If under control, these factors can decrease the incidence and mortality of cancers, including colorectal cancer.

Physical inactivity can increase the prevalence of obesity, which is a risk factor for colorectal cancer. Increased physical activity associated with reduced BMI appears to reduce the risk of colorectal cancer[36,37].

Findings from a case-control study[38] in Northern California showed that a decrease in physical activity associated with an increase in Body Mass Index (BMI) is a justifiable risk factor for an increased incidence of colorectal cancer. Colber et al[39] also showed that the risk of colorectal cancer in inactive workers was significantly higher than that in workers with light or intense physical activity. Researches in Europe and the United States showed that the risk of developing colorectal cancer in people with physical activity is 16% lower than in those with no physical activity[40].

CONCLUSIONS

Considering that the incidence and mortality of colorectal cancer is higher in developed countries, attention to factors associated with the incidence of this disease and lifestyle changes can be effective in reducing the incidence and mortality of this disease. The results of this study emphasize the need for more screening in less developed regions by identifying cases of disease.

Funding:
This article is the result of a research project with the code of ethics IR.KMU.REC.1398.276 of Kerman University of Medical Sciences.

Acknowledgments:
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:
This study has no conflict of interests for the authors

REFERENCES

1. Torre LA, Siegel RL, Ward EM, Jemal A. Global cancer incidence and mortality rates and trends¬–an update. Cancer Epidemiol Biomarkers Prev 2016; 25: 16-27.
2. Fidler MM, Soerjomataram I, Bray F. A global view on cancer incidence and national levels of the human development index. Int J Cancer 2016; 139: 2436-2446.
3. Arnold M, Sierra MS, Laversanne M, Soerjomataram I, Jemal A, Bray F. Global patterns and trends in colorectal cancer incidence and mortality. Gut 2017; 66: 683-691.
4. Center MM, Jemal A, Smith RA, Ward E. Worldwide variations in colorectal cancer. CA Cancer J Clin 2009; 59: 366-378.
5. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2018; 18: e1822.
6. Goodarzi E, Moslem A, Feizhadad H, Jarrahi AM, Adineh HA, Sohrabivafa M, Khazaei Z. Epidemiology, incidence and mortality of thyroid cancer and their relationship with the human development index in the world: an ecology study in 2018. Adv Hum Biol 2019; 9: e162.
7. GLOBOCAN 2018. Available from: http://www.gco.iarc.fr/today/datasources- methods. [Last accessed on 2018 Jan 17].

8. Bray F, Jemal A, Grey N, Ferlay J, Forman D. Global cancer transitions according to the Human Development Index (2008–2030): a population-based study. Lancet Oncol 2012; 13: 790-801.
9. Khazaei S, Rezaeian S, Khazaei Z, Molaeipoor L, Nematollahi S, Lak P, Khazaei S. National breast cancer mortality and incidence rates according to the human development index: an ecological study. Advances Breast Cancer Res2016; 5: 30-36.
10. United Nations Development Programme. Human Development Report 2016. Available from: http://www.hdr.undp.org/en. [Last accessed on 2018 Jan 17].
11. Center MM, Jemal A, Ward E. International trends in colorectal cancer incidence rates. Cancer Epidemiol Biomarkers Prev 2009; 18: 1688-1694.
12. Jemal A, Thun MJ, Ries LA, Howe HL, Weir HK, Center MM, Ward E, Wu XC, Eheman C, Anderson R, Ajani UA, Kohler B, Edwards BK. Annual report to the nation on the status of cancer, 1975–2005, featuring trends in lung cancer, tobacco use, and tobacco control. J Natl Cancer Inst 2008; 100: 1672-1694.
13. Etemad K, Gooya M. National report on registered cancer cases in 2009. Tehran, Iran: Cancer Office, Centre for Disease Control, Deputy for Health, Ministry of Health and Medical Education 2009; pp. 185.
14. Jemal A, Bray F, Center MM, Ferlay J, Ward E, Forman D. Global cancer statistics. CA Cancer J Clin 2011; 61: 69-90.
15. Jemal A, Center MM, DeSantis C, Ward EM. Global patterns of cancer incidence and mortality rates and trends. Cancer Epidemiol Biomarkers Prev 2010; 19: 1893-1907.
16. Kamangar F, Dores GM, Anderson WF. Patterns of cancer incidence, mortality, and prevalence across five continents: defining priorities to reduce cancer disparities in different geographic regions of the world. J Clin Oncol 2006; 24: 2137-2150.
17. Ferrari F, Reis MAM. Study of risk factors for gastric cancer by populational databases analysis. World J Gastroenterol 2013; 19: e9383.
18. Liu Y, Arai A, Obayashi Y, Kanda K, Boostrom E, Lee RB, Tamashiro H. Trends of gender gaps in life expectancy in J apan, 1947–2010: associations with gender mortality ratio and a social development index. Geriatr Gerontol Int 2013; 13: 792-797.
19. Rahimi Pordanjani S, Baeradeh N, Lotfi MH, Pourmohammadi B. Epidemiology of colorectal cancer: incidence, mortality, survival rates and risk factors. Razi J Med Sci 2016; 23: 41-50.
20. Rafiemanesh H, Mohammadian-Hafshejani A, Ghoncheh M, Sepehri Z, Shamlou R, Salehiniya H, Towhidi F, Makhsosi BR. Incidence and mortality of colorectal cancer and relationships with the human development index across the world. Asian Pac J Cancer Prev 2016; 17: 2465-2473.
21. Coleman MP, Quaresma M, Berrino F, Lutz JM, De Angelis R, Capocaccia R, Baili P, Rachet B, Gatta G, Hakulinen T. Cancer survival in five continents: a worldwide population-based study (CONCORD). Lancet Oncol 2008; 9: 730-756.
22. Jung KW, Won YJ, Kong HJ, Oh CM, Shin A, Lee JS. Survival of Korean adult cancer patients by stage at diagnosis, 2006-2010: national cancer registry study. Cancer Res Treat 2013; 45: e162.
23. Mallin K, Palis BE, Watroba N, Stewart AK, Walczak D, Singer J, Barron J, Blumenthal W, Haydu G, Edge SB. Completeness of American Cancer Registry Treatment Data: implications for quality of care research. J Am Coll Surg 2013; 216: 428-437.
24. Sunkara V, Hébert JR. The colorectal cancer mortality-to-incidence ratio as an indicator of global cancer screening and care. Cancer 2015; 121: 1563-1569.
25. Zauber AG. The impact of screening on colorectal cancer mortality and incidence: has it really made a difference? Dig Dis Sci 2015; 60: 681-691.
26. Fedirko V, Tramacere I, Bagnardi V, Rota M, Scotti L, Islami F, Negri E, Straif K, Romieu I, La Vecchia C. Alcohol drinking and colorectal cancer risk: an overall and dose–response meta-analysis of published studies. Ann Oncol 2011; 22: 1958-1972.
27. Moskal A, Norat T, Ferrari P, Riboli E. Alcohol intake and colorectal cancer risk: A dose–response meta-analysis of published cohort studies. Int J Cancer 2007; 120: 664-671.
28. Bouvard V, Loomis D, Guyton KZ, Grosse Y, El Ghissassi F, Benbrahim-Tallaa L, Guha N, Mattock H, Straif K. Carcinogenicity of consumption of red and processed meat. Lancet Oncol 2015; 16: 1599-1600.
29. Huncharek M, Muscat J, Kupelnick B. Colorectal cancer risk and dietary intake of calcium, vitamin D, and dairy products: a meta-analysis of 26,335 cases from 60 observational studies. Nutr Cancer 2008; 61: 47-69.
30. Renehan AG, Tyson M, Egger M, Heller RF, Zwahlen M. Body-mass index and incidence of cancer: a systematic review and meta-analysis of prospective observational studies. Lancet 2008; 371: 569-578.
31. Bardou M, Barkun AN, Martel M. Obesity and colorectal cancer. Gut 2013; 62: 933-947.
32. Harriss D, Atkinson G, Batterham A, George K, Tim Cable N, Reilly T, Haboubi N, Renehan AG, Colorectal Cancer, Lifestyle, Exercise And Research Group. Lifestyle factors and colorectal cancer risk (2): a systematic review and meta-analysis of associations with leisure-time physical activity. Colorectal Dis 2009; 11: 689-701.
33. Walter V, Jansen L, Hoffmeister M, Brenner H. Smoking and survival of colorectal cancer patients: systematic review and meta-analysis. Ann Oncol 2014; 25: 1517-1525.
34. Botteri E, Iodice S, Bagnardi V, Raimondi S, Lowenfels AB, Maisonneuve P. Smoking and colorectal cancer: a meta-analysis. Jama 2008; 300: 2765-2778.
35. Liang PS, Chen TY, Giovannucci E. Cigarette smoking and colorectal cancer incidence and mortality: Systematic review and meta-analysis. Int J Cancer 2009; 124: 2406-2415.
36. Gribovskaja-Rupp I, Kosinski L, Ludwig KA. Obesity and colorectal cancer. Dis Colon Rectum 2011; 24: 229-243.
37. Afshar M, Madani S, Asgari Tarazoj A, Papi SH, Otroshi O, Sadeghi Gandomani H, Rahimi A, H. S. Physical activity and types of cancer. WCRJ 2018; 5: e1164.
38. Slattery ML, Potter J, Caan B, Edwards S, Coates A, Ma KN, Berry TD. Energy balance and colon cancer–beyond physical activity. Cancer Res 1997; 57: 75-80.
39. Colbert LH, Hartman TJ, Malila N, Limburg PJ, Pietinen P, Virtamo J, Taylor PR, Albanes D. Physical activity in relation to cancer of the colon and rectum in a cohort of male smokers. Cancer Epidemiol Biomarkers Prev 2001; 10: 265-268.
40. Eaden J, Abrams K, Mayberry J. The risk of colorectal cancer in ulcerative colitis: a meta-analysis. Gut 2001; 48: 526-535.