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Research

Geographical distribution of incidence and mortality of breast cancer and their association with Human Development Index in Europe

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Abstract

Background: Breast cancer (BC) is the most common cancer malignancy and the important reason for cancer-related mortality in females. The aim of this study was to evaluate the geographical distribution of occurrence and mortality of BC and their association with Human Development Index (HDI) in Europe in 2012. **Methods**: This was an ecologic study to evaluate the relation between Age-Standardized Incidence Rate (ASIR) and Age Standardized Mortality Rate (ASMR) of BC with HDI, using data of GLOBOCAN project and the HDI report. Using SPSS18 statistical analysis software the data of the study was analyzed; the significance level of the tests was considered as P 0.05. **Results**: The highest ASIR of BC was observed in Belgium, Denmark, the Netherlands and the highest ASMR was found in the FYR Macedonia, Serbia, Belgium, respectively. A positive correlation was found between the ASIR of BC and HDI (r= 0.611, p≤ 0.001), life expectancy in birth (r= 0.706, p≤0.001), average education years (r=0.038, p=0.815) and gross national income per capita (r= 0.719, p≤0.001). Moreover, there was negative correlation between the ASMR of BC and HDI (r= 0.464, p= 0.003), life expectancy at birth (r= 0.416, p=0.008), average education years (r= 0.277, p= 0.083) and gross national income per capita (r= 0.255, p= 0.112). Moreover, it is expected that the number of incidence and mortality from BC is increased within 2012-2035 in European countries. **Conclusion**: There is a positive correlation between the ASIR of BC and HDI. Moreover, there is a negative correlation between ASMR of BC with HDI. Therefore, the results of this study indicate the importance of using HDI as factors affecting the ASIR and ASMR of BC.

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1. Background

Breast cancer (BC) is the most common cancer malignancy and the important reason for cancer related-mortality in females [1]. Distribution of new cases of BC was very various in the world, hence, the minimum incidence observed in Asia with Age-Standardized Incidence Rate (ASIR) was 29.1 per 100,000 women and the maximum in Northern America with ASIR was 91.6 per 100,000 women [2,3]. In 2012, in European countries, there were an estimated 463,800 cases of new BC and 131,200 cases of BC-related deaths. In the United States, almost 5% of patients with BC are identified with metastatic disease at first presentation [4]. Moreover, a recent study showed that about 10% of patients diagnosed with early-stage of BC developed metastatic illness within an average of 5.7 years follow-up [5].

However, in recent years deaths from BC are declining in Australia, North America, and Western and most Nordic European countries [6–8]. After more than 20 years of severe mammography screening programs in some of these countries, it is still difficult to determine the amount of the detected decrease in mortality of BC attributed to prior diagnosis or to enhance the management programs. This trouble arises from the limited capacity of observational studies to indicate the effects of primary diagnosis, treatment, and output of healthcare systems on the mortality [9].

Early detection of cancer is vital to decrease the mortality rate and to increase the survival rate of disease [10]. The survival rate of BC is different in the world based on the regional location and socio-economic status [11], hence, in the low-income countries it was less than 40%, and in the high-income countries, it was more than 80%. The low survival of BC in developing countries was related to deficiency of diagnostic and treatment programs [12].

Socioeconomic factors are related to cancer incidence and mortality through complex and changeable pathways. Human Development Index (HDI) is one of the most significant known indicators of socioeconomic factors. The HDI was recommended by UNDP as an indicator for evaluating and comparing the nations in three human aspects including life expectancy at birth, average schooling years and gross national income per capita. Based on HDI, countries are allocated into four classes: Countries with very high HDI (HDI$\geq$ 0.9), countries with high HDI (0.9>HDI$\geq$0.8), countries with Medium HDI (0.8>HDI>0.5), and countries with low HDI (HDI$\leq$0.5) [13]. In the present study, HDI was used as an indicator of socioeconomic factors [14].

In a study conducted in Asia, a positive relation was found between ASIR of BC and HDI. However, this relationship between ASMR and HDI wasn't significant [15] . Similarly in other studies the association between incidence and mortality of other cancers and HDI were examined [16–21]. In most of these studies, a significant association was observed between ASIR, ASMR, and HDI. Therefore, in this study, we investigate the geographical distribution and predict the trend of incidence and mortality of BC and their association with Human Development Index (HDI) in Europe, using data of GLOBOCAN project and the human development index report.

2. Methods

This ecologic study conducted in European countries for appraisement of the correlation among the Age-Standardized Incidence Rate (ASIR) and Age Standardized Mortality Rate (ASMR), and Human development index (HDI) and its components including the average education years, life expectancy at birth, and gross national income per capita. Information on the ASIR for each of European countries for 2012 were acquired from the GLOBOCAN project of World Health Organization (WHO), which is accessible from (http://globocan.iarc.fr/Default.aspx), and statistics on the HDI was gained from the Global report of Human Development index in 2013 [13], that counting definite evidence about the HDI and its components for each of country in the word for 2012.

The method for estimation of the ASIR and ASMR in the GLOBOCAN project

In the GLOBOCAN project, the estimation methods of ASIR and ASMR are particular for each country; therefore, quality of the estimate for each country depends on the quality and the extent of data available for each country. Hence, since methods in every country are specific, determining an overall quality score for the ASIR and ASMR estimations is almost impossible. A detailed description of the material and methods utilized in this scheme provided in previous reports [2].

Human development index (HDI)

In the current study, Human development index (HDI) was used as an indicator of socioeconomic factors [14]. HDI is a complex measure of indicators along with three dimensions including health, education, and standard of living. The HDI is the geometric average of normalized indices for every three dimensions. The health dimension is measured with life expectancy at birth; the education dimension is evaluated by average schooling years for adults and expected schooling years for children, the standard of living dimension is evaluated by gross national income per capita. The scores for HDI dimension indicator are then combined into a complex index using the geometric average [13].

Statistical analysis

In the present study, the correlation bivariate method was used to evaluate the correlation between ASIR and ASMR with HDI, and its components including; average education years, life expectancy at birth, and gross national income per capita. In GLOBOCAN project, the estimated number of new cases and deaths of BC in a region in 2015, 2020, 2025, 2030 and 2035 is calculated by multiplying the age-specific rates estimated for 2012, by the corresponding expected population for 2015, 2020, 2025, 2030 and 2035. In this study, the statistical significance was considered as $P < 0.05$. Whole stated P-values are two-sided. The SPSS (Version 18.0, SPSS Inc.) was used to analyze the study data.

3. Results

Overall in 2012, European countries have recorded 458718 cases of BC, in which 5 countries with the highest number of BC are as the following: Germany with 71623 cases, Russian Federation with 57502 cases, the United Kingdom with 52399 cases, Italy with 50658 cases and France (metropolitan) with 48763 cases, that these five countries totally allocated 280945 cases (61.24%) of BC to themselves.

Furthermore, in European countries in 2012, 131347 cases of deaths occurred caused by BC, among which the five countries with the highest death number are as the following; Russian Federation with 24544 cases, Germany with 16828 cases, Italy with 12796 cases, France (metropolitan) with 11933 cases and the United Kingdom with 11679 cases. These five countries allocated 77780 cases (59.21%) of BC mortality to themselves.

The five countries that have the highest ASIR of the BC per hundred thousand people are as the following; Belgium with 111.9, Denmark with 105, the Netherlands with 99, Iceland with 96.3, and the United Kingdom with 95. In contrast, five countries with the lowest ASIR of the BC were Bosnia Herzegovina with 37.4, the Republic of Moldova with 38.7, Ukraine with 41.3, Greece with 43.9, and Russian Federation with 45.6. The number, crude and standardized incidence rates of the BC in European countries based on sex are presented in **Table 1** . The countries with the highest and the lowest ASIR in both sexes are observed in **Table 1** and **Figures 1 and 3**.

The five countries with the highest ASMR from BC per hundred thousand people are as the following: FYR Macedonia with 25.5, Serbia with 22, Belgium with 20.3, Montenegro with 20.2 and Ireland with 19.1. In contrast, the five countries with the lowest ASMR from BC are as the following: Spain with 11.8, Bosnia Herzegovina with 12, Norway with 12.5, the Czech Republic with 12.8 and Slovakia with 13.1 **Table 1Figures 2 and 3**.

In 2012, some 458718 new cases of BC were observed in the European countries, that 260436 cases (56.77%) are in the age group under 65 years old and 198282 cases (43.23%) are in the age group of 65 years old and higher. According to the forecasts, it is expected that in the years 2015, 2020, 2025, 2030 and 2035 the number of new cases, would be 471724, 487517, 501978, 514408 and 521284, respectively, indicating that over these years the number of new BC cases,

Table 1. Number, crude, and ASIR of BC in European countries in 2012

Estimated incidence, all ages				Estimated mortality, all ages			
Population	**Numbers**	**Crude Rate**	**ASR (W)**	**Population**	**Numbers**	**Crude Rate**	**ASR (W)**
Belgium	10337	188.0	111.9	FYR Macedonia	431	41.8	25.5
Denmark	5224	185.4	105.0	Serbia	2039	41.0	22.0
The Netherlands	13895	165.2	99.0	Belgium	2523	45.9	20.3
Iceland	225	138.1	96.3	Montenegro	102	31.6	20.2
United Kingdom	52399	164.5	95.0	Ireland	704	30.8	19.1
Ireland	2899	126.8	92.3	Denmark	1198	42.5	18.8
Germany	71623	171.5	91.6	Ukraine	8123	33.5	18.4
Italy	50658	162.9	91.3	Republic of Moldova	550	29.7	18.3
France (metropolitan)	48763	149.8	89.7	Malta	77	36.5	18.1
Finland	4477	162.9	89.4	The Netherlands	3163	37.6	18.0
Luxembourg	360	137.0	89.1	Latvia	433	35.9	17.6
Malta	314	148.7	85.9	Russian Federation	24544	32.0	17.2
Switzerland	5750	146.4	83.1	Bulgaria	1391	36.4	17.2
Sweden	6624	139.1	80.4	United Kingdom	11679	36.7	17.1
Cyprus	604	109.3	78.4	Croatia	920	40.4	16.7
FYR Macedonia	1152	111.7	76.2	France (metropolitan)	11933	36.7	16.4
Norway	2887	116.6	73.1	Lithuania	607	34.4	16.3
Czech Republic	6854	127.5	70.3	Hungary	1914	36.6	16.2
Serbia	5422	109.1	69.0	Albania	323	20.0	16.0
Austria	5254	121.9	68.0	Italy	12796	41.2	15.8
Portugal	6088	110.4	67.6	Estonia	258	35.8	15.7
Spain	25215	106.6	67.3	Slovenia	420	40.3	15.6
Slovenia	1258	120.8	66.5	Germany	16828	40.3	15.5
Croatia	2641	116.1	60.9	Romania	3244	29.4	15.2
Montenegro	261	81.0	59.7	Cyprus	132	23.9	14.9
Bulgaria	3928	102.7	58.5	Iceland	39	23.9	14.4
Slovakia	2643	93.9	57.5	Austria	1512	35.1	14.4
Hungary	5094	97.5	54.5	Belarus	1263	24.8	14.2
Albania	1022	63.3	53.9	Greece	2138	37.1	14.1
Latvia	1145	95.0	52.1	Poland	5373	27.1	13.8
Poland	17259	87.0	51.9	Switzerland	1196	30.4	13.6
Estonia	658	91.2	51.6	Finland	860	31.3	13.6
Romania	8981	81.5	50.0	Sweden	1450	30.5	13.4
Lithuania	1479	83.8	48.7	Luxembourg	72	27.4	13.1
Belarus	3781	74.1	45.9	Portugal	1570	28.5	13.1
Russian Federation	57502	75.0	45.6	Slovakia	698	24.8	13.1
Greece	4934	85.6	43.9	Czech Repulic	1617	30.1	12.8
Ukraine	16471	67.9	41.3	Norway	635	25.7	12.5
Republic of Moldova	1104	59.7	38.7	Bosnia Herzegovina	429	22.1	12.0
Bosnia Herzegovina	1152	59.2	37.4	Spain	6075	25.7	11.8

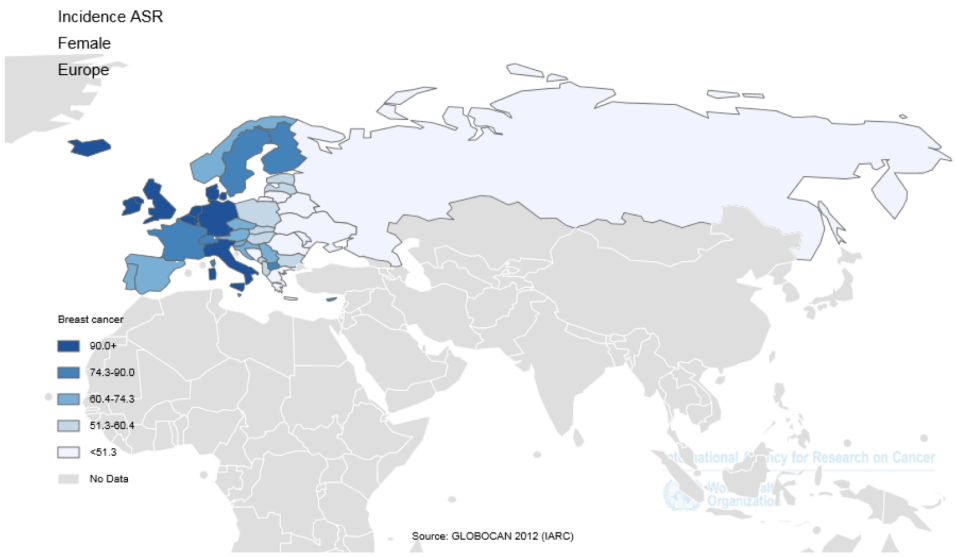

Figure 1. Distribution of the ASIR of BC in European countries in 2012.

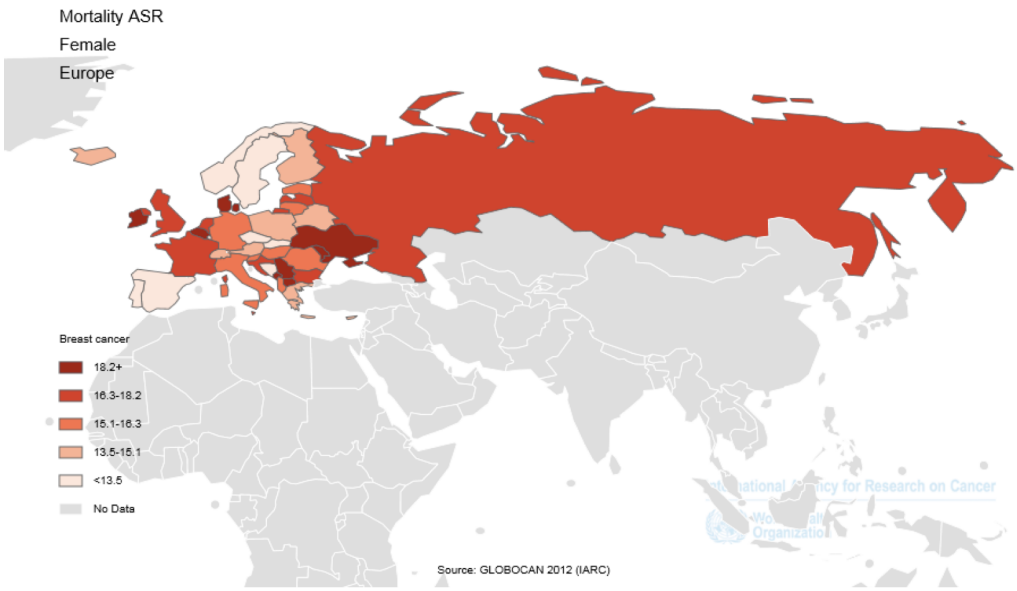

Figure 2. Distribution of ASMR of BC in European countries in 2012.

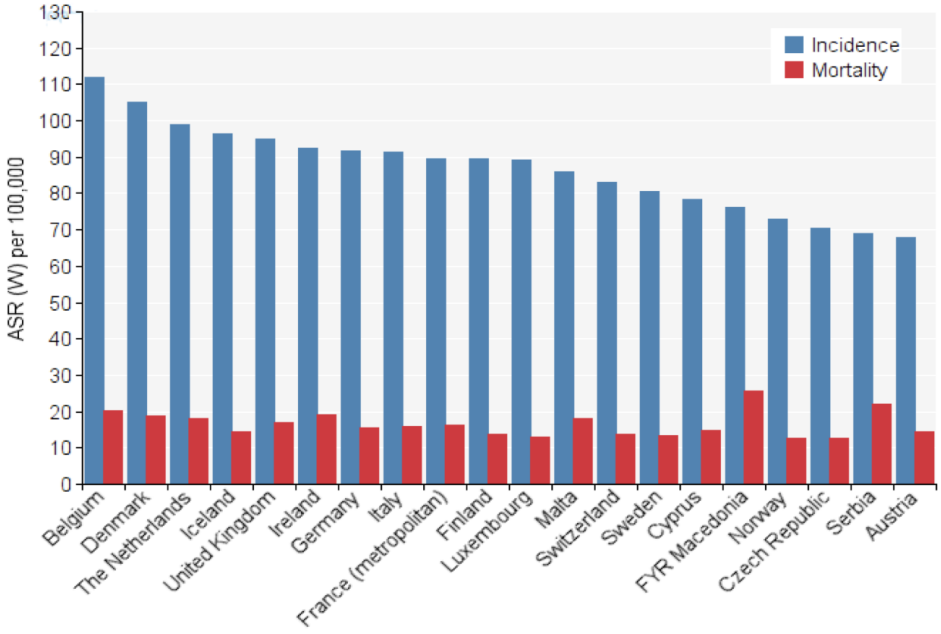

Figure 3. ASIR and ASMR from BC in European countries, in 2012.

increased to 13006, 28799, 43260, 55690 and 62566 cases, respectively, compared to 2012. In fact, over these years the number of new cases is increased to 02.83%, 06.27%, 09.43%, 12.14% and 13.63%, respectively. Although it is predicted that the number of new cases increases within 2012 and 2035, it is predictable that this increase will be more in the age group of 65 years and higher, nonetheless in the age group under 65 years the number of cases will be reduced.

Furthermore, in 2012, about 131347 cases of death were observed in European countries, among which 51310 cases (39.06%) are in the age group under 65 years, and 80037 cases (60.93%) are in the age group of 65 years and higher. According to the predictions, it is expected that in the years 2015, 2020, 2025, 2030 and 2035 the number of death cases, would be 135940, 141053, 147570, 154879 and 161088 cases, respectively, indicating that over these years the number of deaths from the disease increased to 4593, 9706, 16223, 23532 and 29741 cases, compared to 2012. In fact, the number of death increases to 03.49%, 07.38%, 12.35%, 17.91% and 22.64%, respectively. Although it is expected that the number of deaths from BC to increase within 2012 and 2035, it is predictable that this increase will be observed in the age group of 65 years and higher and the number of death from BC will reduce in the age group under 65 years **Table 2** .

In **Table 3** , the respective value of the HDI and its components were shown for each European country that is arranged based on the HDI index. Thus in Europe, countries are classified regarding HDI as the following, so that 29 countries classified as a very high category, nine countries as a high category and two countries are classified as the medium category.

ASIR and HDI

A positive statically significant correlation equal to 0.611 was found between the ASIR of BC and HDI ($p \leq 0.001$). Moreover, a correlation was observed between the components of the HDI and ASIR. So that the ASIR with life expectancy in birth had a positive correlation of 0.706 ($p \leq 0.001$), positive correlation of 0.038 with the average education years ($p=0.815$) and it had a positive correlation of 0.719 ($p \leq 0.001$) with gross national income per capita **Figure 4**.

ASMR and HDI

Furthermore, between the ASMR of BC and HDI, a negative correlation of 0.464 was observed, that this association was statistically significant ($p=0.003$). Moreover, a correlation was observed

Table 2. Estimated number of morbidity and mortality from BC in Europe in 2012-2035

Year	Age group	Estimated number of new cancers	Age group	Estimated number of cancer deaths
2012		458718		131347
	ages < 65	260436	ages < 65	51310
	ages >= 65	198282	ages >= 65	80037
2015		471724		135940
	ages < 65	264338	ages < 65	52458
	ages >= 65	207386	ages >= 65	83482
	Demographic change	13006		4593
	ages < 65	3902	ages < 65	1148
	ages >= 65	9104	ages >= 65	3445
2020		487517		141053
	ages < 65	262578	ages < 65	52386
	ages >= 65	224939	ages >= 65	88667
	Demographic change	28799		9706
	ages < 65	2142	ages < 65	1076
	ages >= 65	26657	ages >= 65	8630
2025		501978		147570
	ages < 65	259061	ages < 65	51719
	ages >= 65	242917	ages >= 65	95851
	Demographic change	43260		16223
	ages < 65	-1375	ages < 65	409
	ages >= 65	44635	ages >= 65	15814
2030		514408		154879
	ages < 65	253470	ages < 65	50526
	ages >= 65	260938	ages >= 65	104353
	Demographic change	55690		23532
	ages < 65	-6966	ages < 65	-784
	ages >= 65	62656	ages >= 65	24316
2035		521284		161088
	ages < 65	248303	ages < 65	49736
	ages >= 65	272981	ages >= 65	111352
	Demographic change	62566		29741
	ages < 65	-12133	ages < 65	-1574
	ages >= 65	74699	ages >= 65	31315

Population predictions were extracted from the United Nations, World Population Prospects, the 2012 revision. Using age-specific rates and corresponding populations for 10 age-groups, the numbers are computed. GLOBOCAN 2012 (IARC) - 15.3.2016

Table 3. Human developmentindex (HDI) in European countries in 2012

HDI status	Population	HDI	Life expectancy at birth	Mean Schooling Year	Gross National Income per capita
Very high human development	Norway	0.955	81.3	12.6	48688
	The Netherlands	0.921	80.8	11.6	37282
	Germany	0.92	80.6	12.2	35431
	Ireland	0.916	80.7	11.6	28671
	Sweden	0.916	81.6	11.7	36143
	Switzerland	0.913	82.5	11	40527
	Iceland	0.906	81.9	10.4	29176
	Denmark	0.901	79	11.4	33518
	Belgium	0.897	80	10.9	33429
	Austria	0.895	81	10.8	36438
	France (metropolitan)	0.893	81.7	10.6	30277
	Finland	0.892	80.1	10.3	32510
	Slovenia	0.892	79.5	11.7	23999
	Spain	0.885	81.6	10.4	25947
	Italy	0.881	82	10.1	26158
	Luxembourg	0.875	80.1	10.1	48285
	United Kingdom	0.875	80.1	9.4	32538
	Czech Republic	0.873	77.8	12.3	22067
	Greece	0.86	80	10.1	20511
	Cyprus	0.848	79.8	9.8	23825
	Malta	0.847	79.8	9.9	21184
	Estonia	0.846	75	12	17402
	Slovakia	0.84	75.6	11.6	19696
	Hungary	0.831	74.6	11.7	16088
	Poland	0.821	76.3	10	17776
	Lithuania	0.818	72.5	10.9	16858
	Portugal	0.816	79.7	7.7	19907
	Latvia	0.814	73.6	11.5	14724
	Croatia	0.805	76.8	9.8	15419
High human development	Belarus	0.793	70.6	11.51	13385
	Montenegro	0.791	74.8	10.5	10471
	Russian Federation	0.788	69.1	11.7	14461
	Romania	0.786	74.2	10.4	11011
	Bulgaria	0.782	73.6	10.6	11474
	Serbia	0.769	74.7	10.2	9533
	Albania	0.749	77.1	10.4	7822
	Ukraine	0.74	68.8	11.3	6428
	Bosnia Herzegovina	0.735	75.8	8.3	7713
Medium human development	Republic of Moldova	0.66	69.6	9.7	3319
	FYR Macedonia	0.59	69.6	5.6	3557

between the components of the HDI and ASMR, so that the ASMR with life expectancy at birth had a negative correlation of 0.416 (p=0.008), a negative correlation of 0.277 (p=0.083) with the average education years and it had negative correlation equal to 0.255 (p=0.112) with gross national income per capita **Figure 5**.

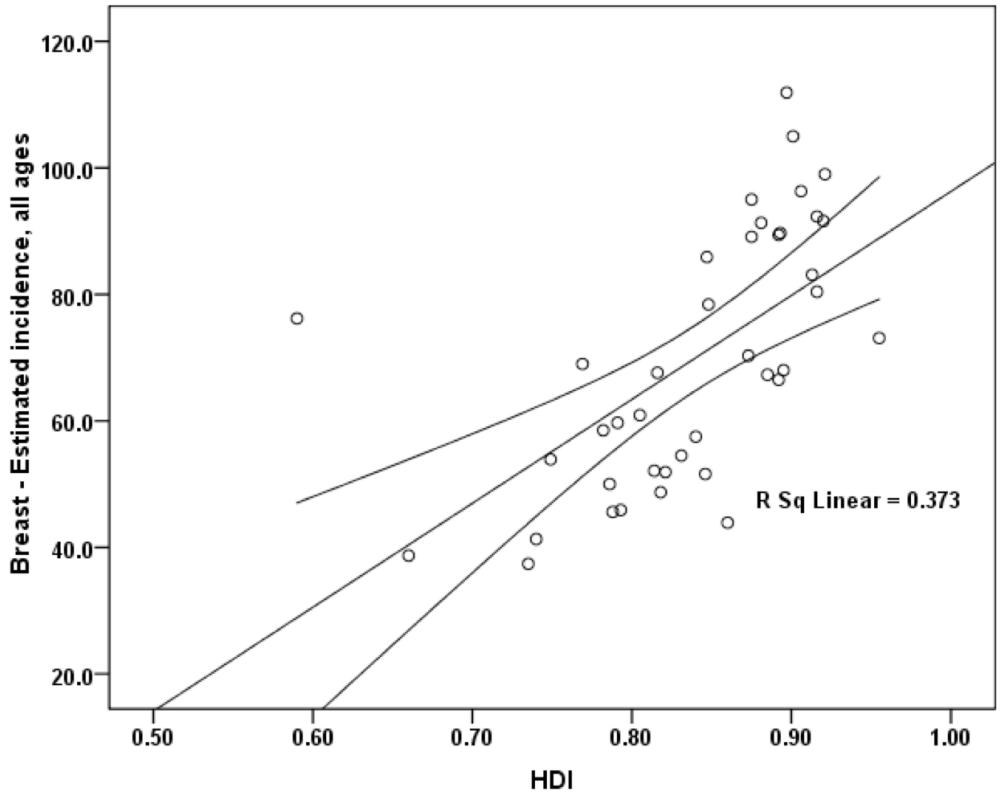

Figure 4. Correlation between HDI and ASIR of BC in European countries in 2012.

4. Discussion

In the present study geographical distribution of incidence and mortality of BC and their association with the HDI in European countries in 2012 were examined. Among European countries the highest ASIR of the BC were observed in Belgium, Denmark, the Netherlands, Iceland, and the United Kingdom, respectively. In addition, the highest ASMR from BC was observed in FYR Macedonia, Serbia, Belgium, Montenegro, and Ireland, respectively. We found that there is a positive correlation between ASIR of BC and HDI and their component. Moreover, there is a negative correlation between the ASMR of BC and HDI and its components. Moreover, it is anticipated that within 2012 and 2035, the number of new cases and the number of deaths caused by BC in the age group of 60 and higher has been increased and it has been declined in the age group under 65 years.

Our results showed that the occurrence of BC in Europe was related to HDI and its components [13]. Among European countries, Belgium with 111.9 per 100,000, Denmark with 105 per 100,000, the Netherlands with 99 per 100,000, Iceland with 96.3 per 100,000, and the United Kingdom with 95 per 100,000 had the highest ASIR of BC. All these countries were in the very high HDI categories. In contrast, in countries such as Bosnia Herzegovina with 37.4 per 100,000,

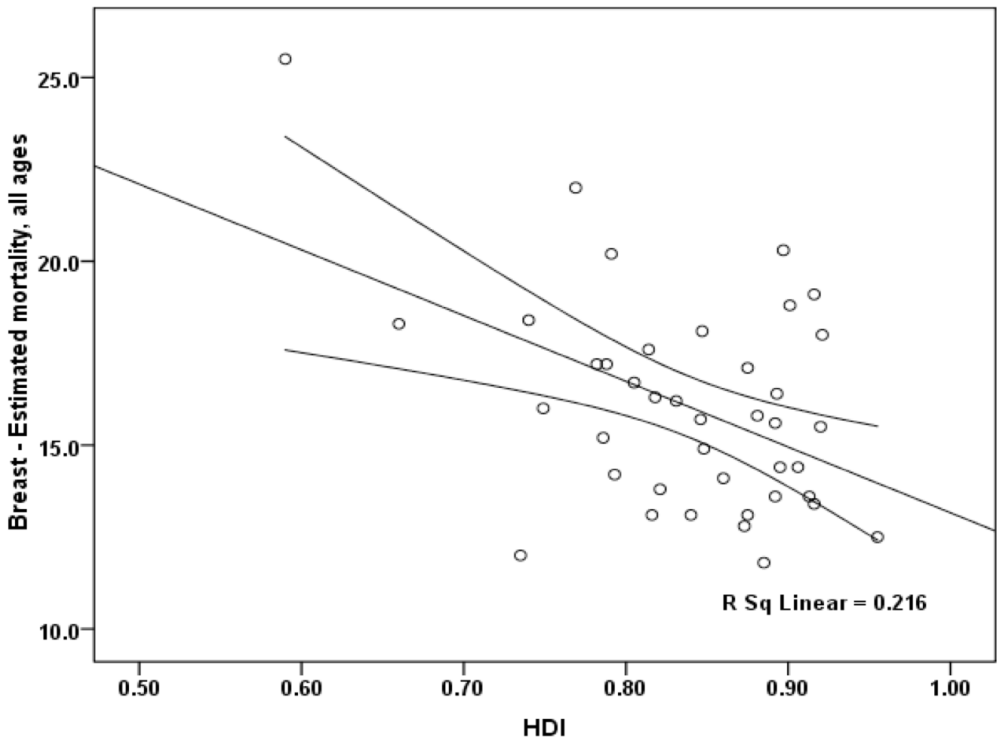

Figure 5. Correlation between HDI and ASMR for BC in European countries in 2012.

the Republic of Moldova with 38.7 per 100,000, Ukraine with 41.3 per 100,000, Greece with 43.9 per 100,000, and Russian Federation with 45.6 per 100,000 the lowest ASIR was observed. However, among these countries, only Greece was in the very high HDI category.

Life expectancy at birth is one of the HDI dimensions [13]. It is directly associated with the occurrence of cancer as well as BC. The risk of chronic diseases such as cancer is increased along with the country development, the removal of competing causes of death, and increasing of life expectancy. This can be associated with increasing the exposure time to risk factors in individuals [22]. In the study conducted in Asian countries regarding BC and HDI, a significant correlation was observed between the ASIR of BC and life expectancy at birth [15].

The second component of HDI is average schooling years. Studies indicated the existence of a positive relationship between average schooling years and individuals' behavior [23]. Increasing the knowledge, education, and employment, women probably perform breast self-examination, thus, looking for diagnostic methods significantly is increased [24]. Hence, in these countries, BC is diagnosed much earlier compared to the countries with lower knowledge levels. In our study, no significant relationship was found between average schooling years and ASIR and ASMR of BC. However, in the study of Ghoncheh et al., in Asia, a significant correlation was observed between ASIR of BC and average schooling years, but the relation between average schooling years and ASMR wasn't significant [15].

The third HDI component is gross national income per capita. According to the report of the World Health Organization (WHO), increasing income and improving the living standards in developing countries led to the intensification in the incidence of BC [25]. This may be caused by the longer life, higher exposure to risk factors, eating more fatty foods and obesity, and lower pregnancy rates [14]. With the increasing development, the incidence of cancers such as BC is increased, and the cancers associated with infectious agents are reduced [14]. Similar to this study, in the study of Ghoncheh *et al.*, in Asia, a significant correlation was observed between ASIR of

BC and gross national income per capita [15]. In high-income countries, the advantage of better diagnostic methods significantly is better compared to the other countries [11]. In fact, diagnosis of cancer in high-income countries is conducted better than low-income countries. In other words, some of BC cases in low-income countries weren't diagnosis and report properly.

Among European countries, the five countries with the lowest ASMR of BC are as the following: Spain, Bosnia Herzegovina, Norway, the Czech Republic and Slovakia, respectively. In five countries with the lowest ASMR from BC except for Bosnia Herzegovina, all other countries were in very high human development category. There was a significant negative linear relationship between ASMR and HDI of BC. In the study of Gonzaga *et al*., in Brazil, there was a significant relationship between HDI and cancer mortality [26]. However, in the study of Ghoncheh *et al*., in Asia, there was not a significant correlation between the ASMR of BC and HDI and its components [15].

The present study involves some advantages. The first advantage is that the data include perfect integrity since we studied all European countries. The second advantage is the introduction of HDI and its components as risk factors for incidence and mortality of BC in European countries which can help the risk factors determination of this disease. The third advantage is the novelty of findings since we couldn't find a study indicating the relationship between the ASIR and ASMR of BC with HDI and its components in European countries.

However, this study includes some limitations. The first limitation is that this study was an ecological study and its results can be interpreted solitary at the population level. Therefore, the ascription of the consequences of this study to individual levels leads to happening the ecological fallacy. The second limitation of this study was different in cancer data collection, diagnosis, and care method among countries entered in the study. Therefore, it is presented that analogous studies in other parts of the world must be conducted so that the association between the ASIR and ASMR of BC and HDI in these areas can be inspected.

5. Conclusions

According to the results of this study, it is expected that the number of incidence and mortality from BC is increased within 2012 and 2035 in European countries. There are positive correlations between the ASIR of BC with HDI. Moreover, there is a negative correlation between ASMR of BC with HDI. Therefore, the statistics from this study represent the importance of using HDI as factors affecting the ASIR and ASMR of BC.

6. Open Access

7. List of abbreviations

ASIR: Age-Standardized Mortality Rate; **ASMR:** Age-Standardized Incidence Rate; **BC:** Breast Cancer; **HDI:** Human Development Index

8. Ethics approval and consent to participate

Not be applied

9. Competing interests

The authors declare that no competing interests exist.

10. Funding

Not be applied

11. Authors' contributions

All authors contributed to the design of the research. MM, KAB, and HS collected the data. HS, FAB, and AMH conducted analysis and interpretation of data. All authors drafted the first version. MM, AMH edited the first draft. All authors reviewed and commented on the final draft.

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