



GEOGRAPHIC VARIATION AND SECULAR TRENDS OF BREAST CANCER INCIDENCE AND MORTALITY IN THE WORLD

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Abstract – Objective: Breast cancer (BC) is a common cancer among women worldwide, accounting for 16% of the total annual incidence of cancer among women. The present study aimed to investigate and compare the incidence and mortality of BC on the basis of different geographical, political and economic divisions in the world as well as investigating long-term trends of the incidence and mortality of this cancer worldwide.

Materials and Methods: In the present study, we extracted the information on the incidence and mortality of BC in 184 countries from the International Agency for Research on Cancer (IARC) (Project GLOBOCAN, 2012). The present study categorized and presented the information on the Age-Standardized Incidence Rate (ASIR) and Age Standardized Mortality Rate (ASMR) of BC based on the continents, world regions based on the development level, World Health Organization (WHO) regions classification and Human Development Index (HDI).

Results: The highest ASIR of BC was observed in regions with a very high HDI (ASIR=78.2), in PAHO (ASIR=67.6), North America (ASIR=91.6) and more developed regions (ASIR=73.4); and the highest ASMR in regions with a low HDI (ASMR=17), in EMRO (ASMR=18.6), more developed regions (ASMR=14.9) and Africa (ASMR=17.3). The ASIR of BC had an ascending trend and the ASMR of this cancer was decreasing from 1975 to 2010. There was a positive statistical correlation equal to 0.883 between ASMR and ASIR of BC in the world.

Conclusions: There was a significant positive correlation between ASIR and ASMR of BC. The ASIR of BC was increasing in most regions of the world, while the mortality rate was decreasing in the world from 1975 to 2010.

KEYWORDS: Epidemiology, Geographical Distribution, Secular Trends, Breast cancer.



LIST OF ABBREVIATIONS: BC: Breast Cancer, WHO: World Health Organization, IARC: International Agency for Research on Cancer, HDI: Human Development Index, ASIR: Age- Standardized Incidence Rate, ASMR: Age- Standardized Mortality Rate, AFRO: WHO Africa region, PAHO: WHO Americas region, EMRO: WHO East Mediterranean region, EURO: WHO Europe region, SEARO: WHO South-East Asia region, WPRO: WHO Western Pacific region.

INTRODUCTION

Breast cancer (BC) is a common cancer among women worldwide, so that it accounts for 16% of the total annual incidence of cancer among women. This cancer is an important prevalent cause of mortality from cancer among women with more than 500,000 case of mortality with this disease per year. More than 60% of all deaths from this cancer occur in less developed regions of the world¹. Based on data of GLOBOCAN PROJECT in 2008, the Age-Standardized Incidence Rate (ASIR) of BC was 27.1 per 100,000 people in less developed regions and 66.4 in developed regions. Furthermore, the lowest ASIR rate of BC was observed in east Africa (19.3%) and the highest in Western European countries (89.7%)^{1,2}.

Estimates suggest that the number of new cases of BC will be 1.7 million people per year by 2020. In fact, the incidence of BC will increase by 26% in 2020 compared to 2000²⁻⁴. Developing countries account for the largest proportion of the increase in the incidence of BC, as it is expected the incidence and mortality rates of BC will increase by 55% and 58% in developing countries in less than 20 years²⁻⁴. The incidence and mortality rates of BC increased by more than 18% in the United States from 1980 to 2008³. As recent cases of cancer can be late diagnosed in developing countries than developed ones, the 5-year survival rate of BC in these countries is lower than developed countries⁵. Early diagnosis of cancers leads to a significant increase in patients' survival rates and more effective therapeutic approaches. According to studies, the probability of cancer diagnosis at the early stages is directly related to patients' income and education levels⁵⁻⁷.

Risk factors of BC are as follows: aging, the first pregnancy at older age, non-marriage and late menopause, early menarche, consumption of oral contraceptive pills, obesity, physical inactivity and drinking alcohol⁸⁻¹¹. In a great number of world's advanced countries, the incidence of BC significantly increased due to screening mammography programs in the early twentieth century. However, there was a decline of 7.6% in the incidence of BC in the US from 2002 to 2003, when the decrease in the incidence of BC was attributed to the reduced consumption of the postmenopausal hormone therapy¹²⁻¹⁴. However, such a relationship did not exist

in Latin America¹⁵. The standardized age-specific incidence and mortality rates of BC were 43.1 and 12.9 respectively in the world in 2012¹⁶. Since the incidence and mortality of BC rise with aging, it is expected that they will increase in the world in the coming years due to population growth and an increase in the middle aged and elderly groups^{6,7,17}. Given the high global incidence and mortality of BC and high costs of screening and treatment programs for patients as well as different distribution of risk factors of this disease, and since the proper understanding of its distribution and trend underlies any appropriate planning and policy to reduce its burden, the incidence and mortality of this disease should be accurately and steadily evaluated and compared at the international level to view the current status and design and implement long-term strategic plans to reduce its burden¹⁸. In developed countries, a great number of studies have been conducted on distribution of cancers and their risk factors at national and regional levels, and their results have been reported at appropriate intervals¹⁹⁻²². However, there aren't many studies on geographical distribution of BC in the world¹⁷. Therefore, geographical differences in distribution of this disease have not been fully understood based on division of the World Health Organization (WHO), development level, continents, and the human development index (HDI). The present study aimed to investigate and compare the incidence and mortality of the BC on the basis of different geographical, political and economic divisions in the world as well as investigating long-term trends of the incidence and mortality of this cancer worldwide.

MATERIALS AND METHODS

In the present study, we extracted the information on the incidence and mortality of BC in 184 countries from the International Agency for Research on Cancer (IARC) (Project GLOBOCAN, 2012). GLOBOCAN is a database on various types of cancers and it is created by the WHO. It covers information on the number, raw rates, and age ASIR, prevalence and ASMR for different regions and countries. Currently, the available data in GLOBOCAN is known as one of the newest international database on the cancer. Based on the data of GLOBOCAN

project, it is possible to investigate and compare the incidence and mortality of cancer based on the type of cancer, age and gender groups for different regions of the world^{23, 24}. The present study categorized and presented the information on the ASIR and ASMR of BC based on the continents (Africa, Latin America and Caribbean, Northern America, Europe, Oceania, Asia), world regions based on the development level (more developed regions and less developed regions), WHO Region classification (Africa region (AFRO), Americas region (PAHO), East Mediterranean region (EMRO), Europe region (EURO), South-East Asia region (SEARO) and Western Pacific region (WPRO) and HDI level (very high, high, medium, and low). We provided the information about the incidence and mortality of BC based on the number, raw rates and the ASIR and ASMR in 2012. We also expressed raw and ASIR and ASMR of BC per 100,000 people. Geographical distribution map was prepared for the ASIR and ASMR of this disease based on the age-specific rates. Detailed descriptions of applied methods are presented in previous reports²⁵⁻³⁵.

RESULTS

THE ASIR AND ASMR OF BC IN THE WORLD

In general, 1,671,149 new BC cases were diagnosed worldwide in 2012. 47.17% (788,200 cases) occurred in more developed regions and 52.83% (882,949 cases) in less developed regions in the world. 44.71% (747,203 cases) of this disease occurred in regions with very high HDI; 16.86% (281,687 cases) in

regions with high HDI; 29.55% (493,807 cases) in regions with moderate HDI, and 8.28% (147,415 cases) in regions with low HDI. From a total incidence of disease, 8% (133,890 cases) occurred in Africa, 38.95% (650,938 cases) in Asia, 27.45% (458,718 cases) in Europe, 15.1% (19,277 cases) in Oceania, 15.33% (256,222 cases) in North America, and 9.10% (15,2059 cases) in Latin America and the Caribbean. In this year, 521,907 deaths from the BC were diagnosed. 37.86% (197,618 cases) were found in more developed regions and 62.14% (324,289) in less developed regions of the world, 32.14% (169,131 cases) in regions with very high HDI, 18.33% (95,646 cases) in regions with high HDI, 34.90% (182,166 cases) in regions with moderate HDI, and 14.31% (74,678 cases) in regions with low HDI. From the total incidence of disease, 12.1% (63,160 cases) occurred in Africa, 44.26% (231,013 cases) in Asia, 25.17% (131,347 cases) in Europe, 0.83% (4,329 cases) in Oceania, 9.36% (48,850 cases) in North America, and 8.28% (43,208 cases) in Latin America and the Caribbean.

THE ASIR AND ASMR OF BC BASED ON THE CONTINENTS

The ASIR of BC was 43.1 per 100,000 people worldwide. It was 36.2 in Africa, 29.1 in Asia, 69.9 in Europe, 79.2 in Oceania, 91.6 in North America, and 47.2 in Latin America and the Caribbean (Figure 1 and 2).

The ASMR of BC was 12.9 per 100,000 people worldwide. It was 17.3 in Africa, 10.2 in Asia, 15.6 in Oceania, 14.8 in North America, and 13 in Latin America and the Caribbean (Figure 1 and 3).

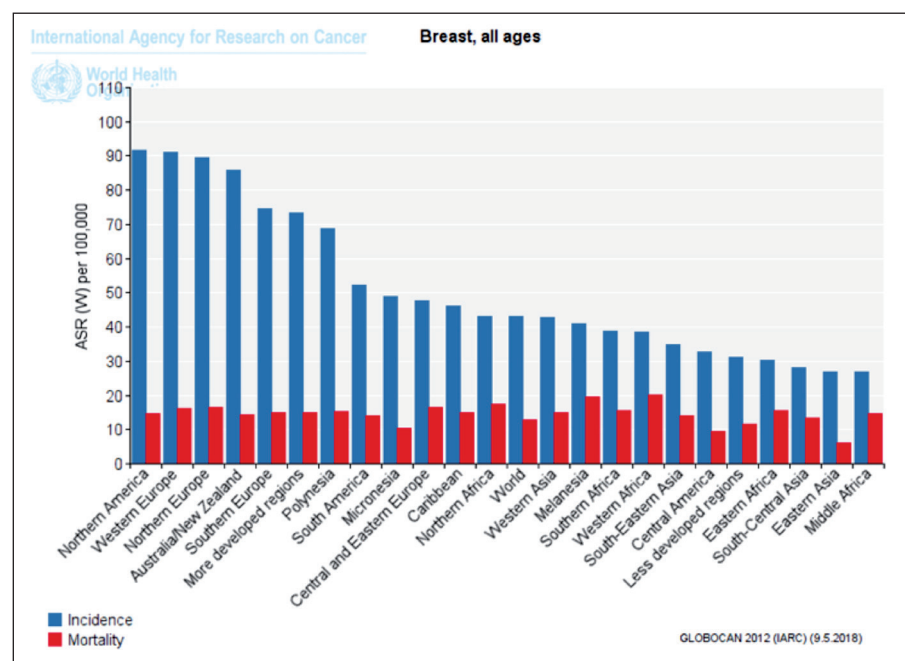


Fig. 1. Areas with the highest ASIR and ASMR of BC in the world in 2012.

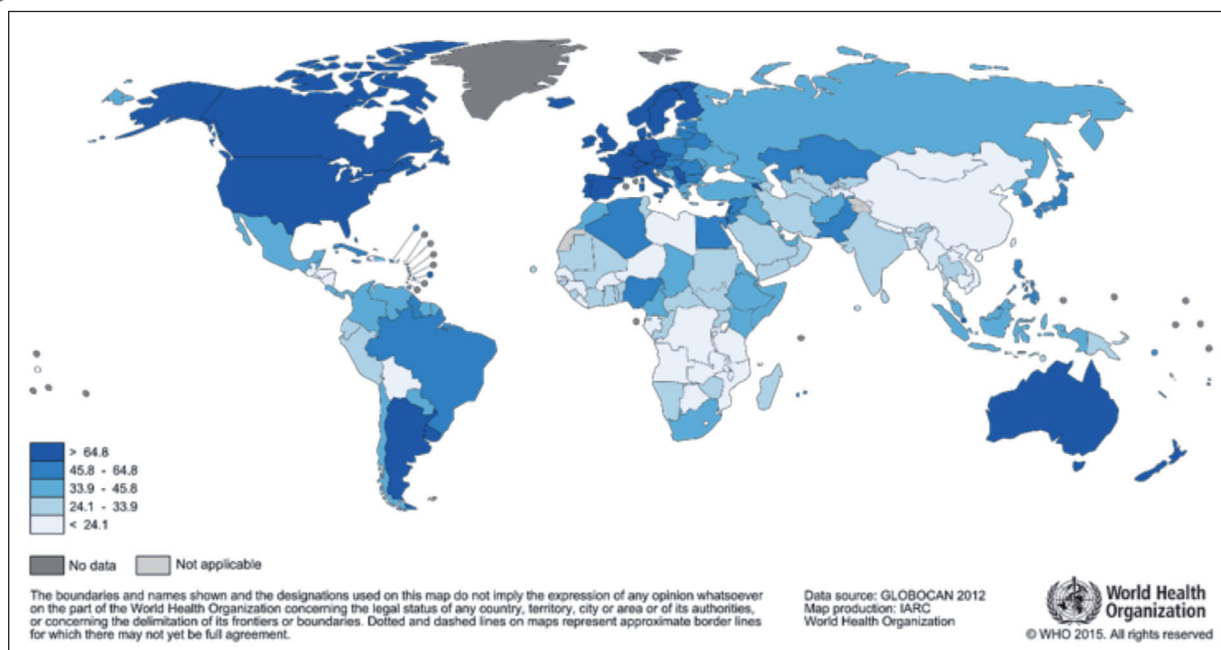
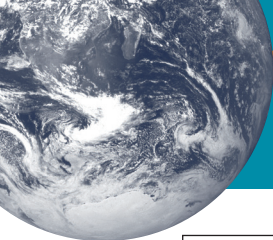


Fig. 2. Distribution of new cases of BC in females in the world in 2012.

THE ASIR AND ASMR OF BC BASED ON THE DEVELOPMENT LEVEL

The ASIR of BC was equal to 73.4 in more developed regions of the world and 31.3 in less developed regions. The ASMR of this cancer was 14.9 in more developed regions and 11.5 in the less developed regions.

THE ASIR AND ASMR OF BC ACCORDING TO THE WHO REGIONS CLASSIFICATION

ASIR of BC was 34.5 in AFRO, 67.6 in PAHO, 41.9 in EMRO, 27.8 in SEARO, 66.5 in EURO, and 28.6 in WPRO. Furthermore, the ASMR of this cancer was 17.2 in AFRO, 14 in PAHO, 18.6 in EMRO, 12.9 in SEARO, 16 in EURO and 7 in WPRO.

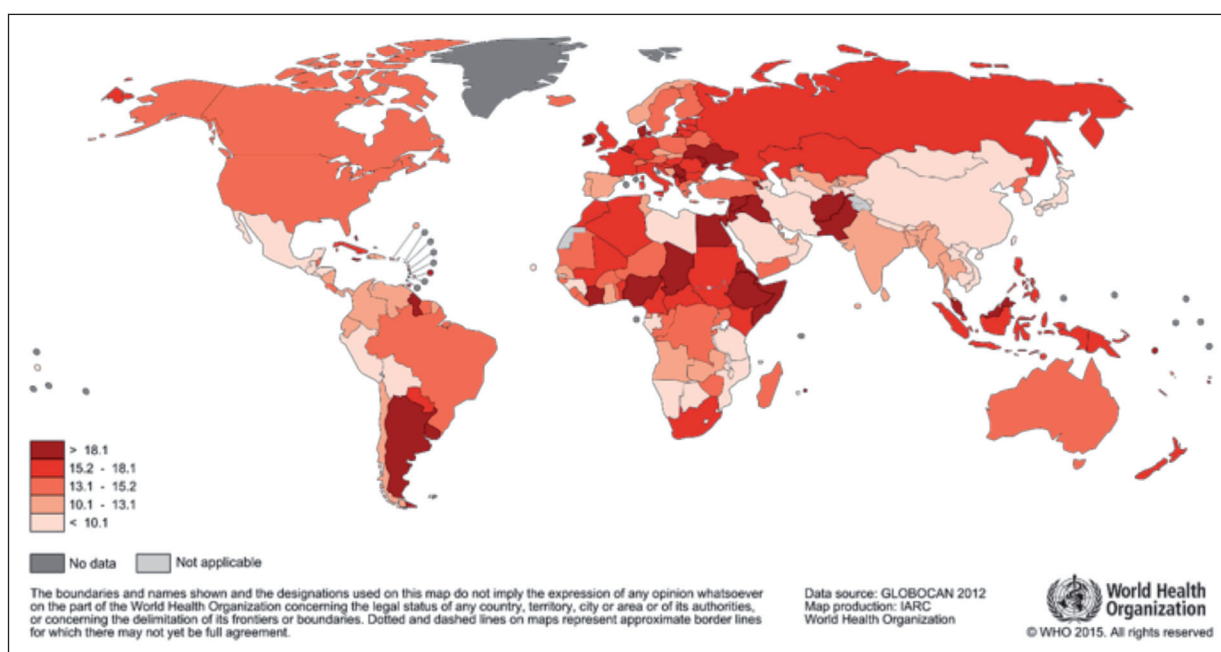


Fig. 3. Distribution of mortality of BC in females in the world in 2012.

THE ASIR AND ASMR OF BC ACCORDING TO THE LEVELS OF HDI

The ASIR of BC was equal to 78.2 in regions with very high HDI, 45.2 in regions with high HDI, 26.5 in regions with medium HDI, and 32.6 in regions with low HDI.

The ASMR of BC was equal to 14.1 in regions with very high HDI, 14.6 in regions with high HDI, 9.8 in regions with medium HDI, and 17 in regions with low HDI (Table 1).

THE TREND OF BC ASIR AND ASMR DURING 1950 TO 2010

The ASIR of BC had an ascending trend from 1975 to 2010, so that the ASIR increased from 60 to more than 100 cases per 100,000 in Denmark, from 40 to 90 in Finland, 20 to 58 in Singapore, and 58 to 83 in Australia (Figure 4), while the ASMR rate was declining in most countries from 1975 to 2010, so that the ASMR of BC decreased from 27 to 19 in Denmark, 15 to 14 in Finland, 19 to 14 in Australia, and 22 to 15 in the US. It seems that the ASMR of BC did not have dramatic decline in Asian countries during this period, and it was increasing in some countries (Figure 5).

RELATIONSHIP BETWEEN ASIR AND ASMR OF BC

The highest ASIR of BC was 111.9 in Belgium, 105 in Denmark, and 99 in the Netherlands, but the lowest ASIR was seen equal to 4.6 in Bhutan, 9 in Lesotho, and 9.4 in Mongolia. Furthermore, the highest ASMR of BC was seen equal to 28.4 in Fiji, 26.3 in Bahamas and 25.9 in Nigeria, and the lowest ASMR was equal to 1.8 in Bhutan, 4.2 in Mongolia and 4.4 in Lesotho. There was a positive and significant correlation between the ASIR and ASMR of BC in worldwide ($r = 0.853$, $p \leq 0.001$) (Figure 6). This correlation was equal to $r = 0.798$ ($p \leq 0.001$) in America, $r = 0.159$, ($p = 0.328$) in Europe, $r = 0.450$ ($p = 0.192$) in Oceania, $r = 0.727$ ($p \leq 0.001$) in Asia, and $r = 0.796$ ($p \leq 0.001$) in Africa.

DISCUSSION

This study was conducted based on data of GLOBOCAN PROJECT by the WHO in the world in 2012. The present study aimed to examine the geographical distribution of incidence and mortality of BC based on geographical, political and economic divisions at the international level. Furthermore, the 35-year trends of ASIR and ASMR of BC were evaluated and compared in different countries from 1975 to 2010. In general, 167,115 new cases of BC were registered and diagnosed in 2012. 17.47%

of them occurred in more developed regions, and 52.83% in less developed regions worldwide. The ASIR of BC per 100,000 people was 43.1 worldwide, 36.2 in Africa, 29.1 in Asia, 69.9 in Europe, 79.2 in Oceania, 91.6 in North America, and 47.2 in Latin America and the Caribbean. The ASIR of BC had an ascending trend from 1975 to 2010. On the other hand, 521,907 deaths from BC were reported during this period, so 37.86% was in more developed regions, and 62.14% in less developed regions of the world. The ASMR of BC was 12.9 worldwide, 17.3 in Africa, 10.2 in Asia, 15.6 in Oceania, 14.8 in North America, and 13 in Latin America and the Caribbean. The ASMR of this cancer was decreasing in most countries. There was a positive statistical correlation equal to 0.883 between ASMR and ASIR of BC in the world. BC is a common cancer among women and the second most common cancer in the world. From a total of 1,671,149 new cases of BC worldwide in 2012, 47.17% (788,200 cases) occurred in more developed regions and 52.83% (882,949 cases) in less developed regions worldwide. According to a research by Curado³⁶ on the incidence and mortality of BC worldwide, more than 1.38 million new cases of BC were diagnosed and recorded in 2008 and they accounted for 10.9% of the total incidence of cancer worldwide. In 2008, a half of newly diagnosed BC cases occurred in developed countries, and another half in developing countries³⁶. Despite the fact that 25% of the world's total population lives in developed regions, these regions account for about 50% of the total newly diagnosed cases probably due to the higher average age of the population, improved diagnostic methods, the high efficiency of disease registration system and implementation of extensive screening programs in these areas³⁷⁻⁴⁰. In 2012, the highest ASIR rates of BC per 100,000 people were observed in Belgium (ASIR= 111.9) and Denmark (ASIR= 105), but the lowest ASMR in Bhutan (ASIR= 4.6) and Mongolia (ASIR= 9.4). Despite the low incidence of this cancer in less developed countries, it is expected that the incidence of BC will also increase due to the industrialization of these societies, increased life expectancy and increased prevalence of obesity and infertility^{8,41}. Nagrani et al⁴² in India showed that the incidence of BC in villagers was lower than those living in urban areas, indicating the impact of lifestyles on the incidence of BC. Given that some of determinants of the incidence of BC have been diagnosed, the society-based preventive programs can reduce the incidence of this disease. The five-year survival rate of BC is very different in various geographical regions of the world, so that the survival rate is about 40% in some Asian and African countries with low-income levels and more than 80% in North America.

TABLE 1. Incidence and mortality of BC in different regions of the world.

<i>Population</i>	<i>Incidence</i>			<i>Mortality</i>			<i>Mortality/incidence</i>
	<i>Numbers</i>	<i>Crude Rate</i>	<i>ASR (W)</i>	<i>Numbers</i>	<i>Crude Rate</i>	<i>ASR (W)</i>	
World	1671149	47.8	43.1	521907	14.9	12.9	0.31
More developed regions	788200	123.2	73.4	197618	30.9	14.9	0.25
Less developed regions	882949	30.9	31.3	324289	11.4	11.5	0.37
Very High Human Development	747203	128.0	78.2	169131	29.0	14.1	0.23
High Human Development	281687	53.2	45.2	95646	18.0	14.6	0.34
Medium Human Development	493807	28.5	26.5	182166	10.5	9.8	0.37
Low Human Development	147415	22.7	32.6	74678	11.5	17.0	0.51
WHO Africa region (AFRO)	99760	22.7	34.5	49061	11.2	17.2	0.49
WHO Americas region (PAHO)	408281	84.6	67.6	92058	19.1	14.0	0.23
WHO East Mediterranean region (EMRO)	99284	32.6	41.9	42228	13.9	18.6	0.43
WHO Europe region (EURO)	494076	106.2	66.5	142979	30.7	16.0	0.29
WHO South-East Asia region (SEARO)	239612	26.4	27.8	109631	12.1	12.9	0.46
WHO Western Pacific region (WPRO)	329762	36.8	28.6	85837	9.6	7.0	0.26
IARC membership (24 countries)	934832	71.9	56.9	256832	19.8	14.3	0.27
Middle-East and Northern Africa (MENA)	81997	37.3	43.0	30387	13.8	16.2	0.37
Africa	133890	25.0	36.2	63160	11.8	17.3	0.47
Sub-Saharan Africa	94378	21.8	33.8	47583	11.0	17.2	0.50
Eastern Africa	33472	18.9	30.4	17028	9.6	15.6	0.51
Middle Africa	10922	16.3	26.8	5984	8.9	14.8	0.55
Northern Africa	39512	38.0	43.2	15577	15.0	17.4	0.39
Southern Africa	10303	34.9	38.9	4047	13.7	15.5	0.39

Continued

TABLE 1 (CONTINUED). Incidence and mortality of BC in different regions of the world.

<i>Population</i>	<i>Incidence</i>			<i>Mortality</i>			<i>Mortality/incidence</i>
	<i>Numbers</i>	<i>Crude Rate</i>	<i>ASR (W)</i>	<i>Numbers</i>	<i>Crude Rate</i>	<i>ASR (W)</i>	
Western Africa	39681	25.0	38.6	20524	12.9	20.1	0.52
Latin America and Caribbean	152059	49.8	47.2	43208	14.1	13.0	0.28
Caribbean	11287	53.1	46.1	3928	18.5	15.1	0.35
Central America	24891	30.7	32.8	7266	8.9	9.5	0.29
South America	115881	57.1	52.1	32014	15.8	14.0	0.28
Northern America	256222	144.5	91.6	48850	27.5	14.8	0.19
Asia	650983	31.4	29.1	231013	11.1	10.2	0.35
Eastern Asia	277054	36.0	27.0	68531	8.9	6.1	0.25
South-Eastern Asia	107545	35.3	34.8	43003	14.1	14.1	0.40
South-Central Asia	223899	25.3	28.2	104669	11.8	13.5	0.47
Western Asia	42485	36.6	42.8	14810	12.8	15.1	0.35
Europe	458718	119.5	69.9	131347	34.2	16.1	0.29
European Union (EU-28)	361608	139.5	80.3	91585	35.3	15.5	0.25
Central and Eastern Europe	123617	79.2	47.7	48717	31.2	16.5	0.39
Northern Europe	78249	153.6	89.4	17915	35.2	16.4	0.23
Southern Europe	100807	125.9	74.5	27473	34.3	14.9	0.27
Western Europe	156045	161.3	91.1	37242	38.5	16.2	0.24
Oceania	19277	102.4	79.2	4329	23.0	15.6	0.22
Australia/New Zealand	17550	127.6	85.8	3620	26.3	14.5	0.21
Melanesia	1376	30.8	41.0	633	14.2	19.7	0.46
Micronesia/Polynesia	351	57.9	59.7	76	12.5	13.1	0.22
Micronesia	128	47.1	48.8	27	9.9	10.4	0.21
Polynesia	223	66.6	68.9	49	14.6	15.4	0.22

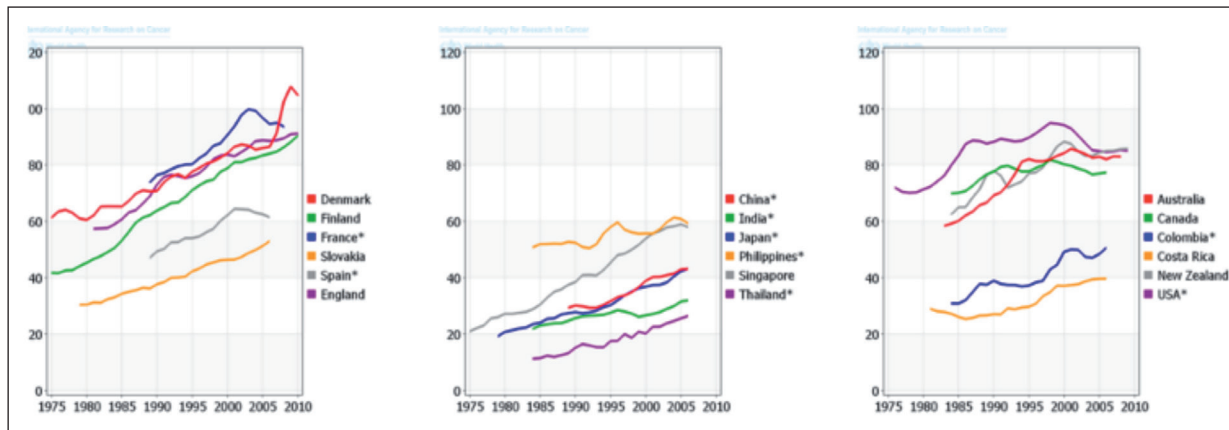
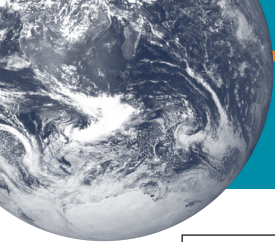


Fig. 4. Trends in the incidence of BC in selected countries: age-standardized rate (W) per 100,000 people.

Results of a number of studies^{41,43,44} indicate that the economic and social status of people has a direct relationship with the diagnosis stage and their survival rate of disease. Therefore, the probability of disease diagnosis at its early stages is higher in people with higher economic status. Given the more effective use of therapeutic methods at these stages and patients' abilities to access appropriate treatment methods, survival rates are higher in these individuals than those with lower social and economic levels⁴⁵. Therefore, it seems that the late diagnosis of disease and limited access to medical facilities are the reasons for high probability of BC mortality in developing countries⁴⁶. In the present study, the highest and lowest incidence of BC was observed in regions with medium and very high HDI, respectively. This finding is consistent with obtained results of other studies in this field^{6,7,17}, so that an increase in the HDI increases the ASIR of BC. The correlation between the HDI and the ASIR of BC was studied in a number of studies^{6,7,17}. Ghoncheh et al⁶ in Asia showed that there was a positive and significant correlation between the

incidence of BC with the HDI ($r = 0.556, p = 0.001$). Similar results were also found by Mohammadian et al⁷ in Europe ($r = 0.611, p \leq 0.001$), and Ghoncheh et al¹⁷ worldwide ($r = 0.725, p \leq 0.001$). The HDI is a complex and multifaceted index that can be calculated on the basis of the life expectancy, mean education level and gross domestic income (GDI) for different regions of the world. This index can be used to examine and compare different regions of the world in terms of economic and social aspects. It seems that the reasons for a significant increase in the incidence of BC in regions with a high HDI are as follows: higher average age of the population, and consequently, the higher proportion of elderly people compared with those with low HDI; more access and use of advanced diagnostic equipment; implementing extensive screening programs; more efficiency of cancer registry systems; higher prevalence of obesity and low activity; and higher average age of marriage in women². The highest ASMR of BC occurs in regions with low HDI, but the lowest rate in regions with very high HDI. Others studies also found a negative correlation between

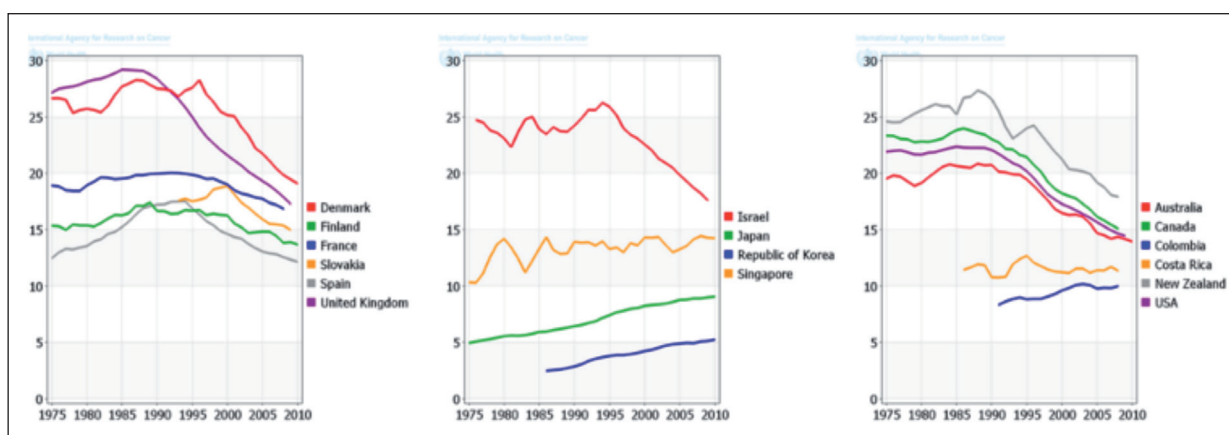


Fig. 5. Trends in mortality from BC in selected countries: age-standardized rate (W) per 100,000 people.

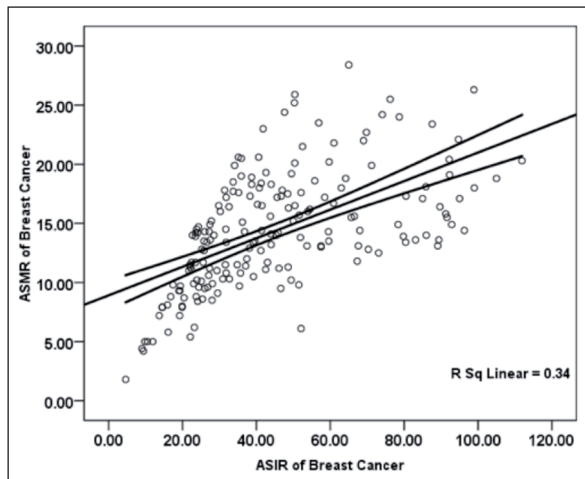


Fig. 6. Correlation of ASIR and ASMR of BC in the world in 2012.

the HDI and ASMR of BC. In fact, an increase in the HDI decreased the ASMR of BC, for instance, Mohammadian et al⁷ found a significant negative correlation between the HDI and the ASMR of BC in European countries ($r = 0.464$, $p = 0.003$), despite the fact that this relationship was not statistically significant in some studies^{6,17}. The quality of recording and reporting the cancer incidence and mortality was not equal in all studied regions, so that recording data on the incidence and mortality of cancer was not population-base in some of regions, and data might be collected from a few regions, or amounts might be measured based on estimates of neighboring countries in some countries with a low or moderate HDI⁶.

CONCLUSIONS

The highest ASIR of BC was observed in regions with very high HDI, in WHO PAHO region, North America and more developed regions; also, the highest ASMR in regions with low HDI, in WHO EMRO region, more developed regions and in Africa. There was a significant positive correlation between ASIR and ASMR of BC. The ASIR of BC was increasing in most regions of the world from 1975 to 2010, while the ASMR was decreasing trend in the world.

AUTHOR CONTRIBUTIONS

All authors contributed to the design of the research. MM, HS, KAB, AS, AA, FAB and AMH extracted the data and summarized it. All authors drafted the first version. HS, KAB, AS, ME, HK and AMH edited the first draft. All authors reviewed, commented and approved the final draft.

CONFLICT OF INTEREST

The authors declare that have no conflicts of interest to disclose.

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